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UNOFFICIAL TRANSCRIPT*
WASHINGTON STATE
PHARMACY AND THERAPEUTICS COMMITTEE MEETING
December 16, 2009
Sea Tac Marriott Hotel
9:00am – 4:00pm

Carol Cordy: Good morning. This is Carol Cordy. We'll bring the meeting to order. Vyn, I think is caught in traffic and will be here soon. So Jeff has some announcements to make. Let's introduce ourselves around and then turn it over to Jeff. Do you want to start down here? Introduce yourself.

Cathy Williams: Sorry. Cathy Williams, Pharmacist Consultant, Board of Pharmacy.

Amy Irwin: Amy Irwin, Pharmacy Program, Washington Medicaid.

Jeff Thompson: Jeff Thompson, Washington Medicaid.

Chuck Agte: Chuck Agte, Washington Medicaid.

Siri Childs: Siri Childs, Pharmacy Administrator, Washington Medicaid.

Jaymie Mai: Jaymie Mai with Labor and Industry.

Doug Tuman: Doug Tuman with Labor and Industry.

Jeff Graham: Jeff Graham, Health Care Authority.

Patti Varley: Patti Varley, P&T.

Janet Kelly: Janet Kelly, P&T.

* For copies of the official audio taped record of this meeting, please contact Regina Chacon at (206)521-2027 pdp@hca.wa.gov.

Carol Cordy: Carol Cordy, P&T.

Jason Iltz: Jason Iltz, P&T.

Alvin Goo: Alvin Goo, P&T.

Barak Gaster: Barak Gaster, P&T.

Regina Chacon: Regina Chacon, Health Care Authority.

Leta Evaskus: Leta Evaskus, Health Care Authority.

Duane Thurman: Duane Thurman, Health Care Authority.

Ray Hanley: Ray Hanley, Health Care Authority.

Carol Cordy: Jeff?

Jeff Graham: Well, we have a few announcements today. We have three members who are leaving this committee. They have served over six years and…our chair is finally arriving here. And two of them are unable to make it today—Bob Bray from Spokane was not able to. And I think Angelo Ballasiotes I think they had some weather problems in Yakima so he isn't able to make it today. But Janet Kelly is here today and this we really appreciate all the good work she's done for us. Unfortunately, she's leaving. She could come back after a year. So it's been very good having her on this committee and we really appreciate all you've done, Janet. Thank you!

Janet Kelly: Thank you.

Jeff Graham: We do have a reappointment to announce today. Ken Wiscomb will be reappointed for a three-year term. And we will make an announcement in the…by the middle of January of the replacements for Angelo, Bob and Janet. So that will be coming out at that time. We are narrowing down those folks right now and we'll have an announcement then. So welcome, Vyn. We're glad you made it through. And we can go ahead…I don't think that…I haven't heard the person come on from North Carolina.

Megan van Noord: Oh, I'm here.

Jeff Graham: Oh, you are? Good. Great. Well, we're ready to start then on the second generation antidepressants. And we'll go from there.

Megan van Noord: Great. Can everyone see the slides?

Jeff Graham: Our slides are up.

Vyn Reese: Right. This is Dr. Reese. Why don't you go ahead?

Megan van Noord: Okay. Great. So I'll be presenting the first preliminary scan report for the fifth update of second generation antidepressants. Your next slide.

A little background information. The last report was completed in October of 2008 and included searches through April of 2008. Okay?

Populations included outpatients with depressive anxiety and/or premenstrual dysphoric disorders. Next slide.

For the included interventions there are 11 antidepressants agents being evaluated which are…can be seen on the slide. And there's also one additional antidepressant, desvenlafaxine, which was FDA approved in February of 2008. Next slide.

Slide 5 was the efficacy and effectiveness outcomes, which include response, remissions, speed of response/remission, relapse, quality of life, functional capacity as well as hospitalization.

The next slide includes harms outcomes, which are listed below. Next slide.

For the literature search to identify relevant citations we searched PubMed from April 2008 through November 11, 2009. We also searched FDA and Health Canada websites for identification of new drugs, indications and safety alerts. Next slide.

For the study selection one reviewer assessed abstracts of citations identified from literature searches for inclusion using the criteria previously described. And onto the results.

Searches results there have been 127 new citations. Of those there are 26 new potentially relevant studies, which are located in Appendix A. A supplemental search was conducted for desvenlafaxine resulting in 26 citations and 3 of the citations were captured in the above search and are potentially relevant studies. There was little overlap between the searches. Of the remaining 23 citations there are 6 new potentially relevant studies, which are located in Appendix E. Next slide.

One new drug was found, desvenlafaxine, which is an SNRI and indicated for the treatment of major depressive disorder. Next slide.

There are no new indications at this time and finally there are no new safety alerts.

Vyn Reese: Thank you very much.

Megan van Noord: No problem.

Vyn Reese: Are there any questions from the committee? I'll take a motion to approve the scan.

Patti Varley: Patti Varley. I move to approve the scan.

Vyn Reese: Is there a second?

Barak Gaster: Barak Gaster. I move to second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The scan is accepted. There are three stakeholders. The first is Casey Eastman. On deck is Steve Cheng and you have three minutes to speak. Dr. Graham will be timing you.

Casey Eastman: Good morning. My name's Casey Eastman and I represent UCB and Venlafaxine extended release tablets. Venlafaxine extended release tablets were approved in July of 2008 for the treatment of major depressive disorder and socializing anxiety disorder. It is not indicated for

panic disorder or generalized anxiety disorder. Approval of the tablets was based on both efficacy and safety data of Effexor XR. Four randomized trials in healthy adults, three single-dose trials and one multi-age trial were demonstrated that bradycardia equivalency of these agents under federal conditions.

In 1984 the Hatch-Watchman Act was passed that allowed for medications to be approved for marketing via a 505B2ANDA. These entities comply…or excuse me, these entities could rely on findings and safety or…and/or efficacy of previously approved products coupled with information needed to support changes in the approved product. The agents must be demonstrated to be bioequivalent. As the name implies Venlafaxine extended release tablets are an extended release tablet formation while Effexor XR is an extended release capsule formation. Due to the difference in dosage formulation, Venlafaxine extended release tablets are not AB rated 2 or a generic of Effexor XR, but are considered by FDA definitions to be a pharmaceutical alternative to Effexor XR.

In addition to the change in dosage formulation, Venlafaxine extended release tablets also come in a single 225 mg tablet formulation, a strength not currently available with Effexor XR. Any patients prescribed 225 mg of Venlafaxine extended release in an extended release formation should be titrated. Some patients may start at 37.5 mg per day after 4 to 7 days dosage should be increased by 75 mg per day before substantially increasing by 75 mg intervals every 4 to 7 days. Both formulations should be taken with food. The capsules may be opened and sprinkled on food while the tablets must be swallowed whole. Clinicians can expect similar efficacy in both Venlafaxine extended release tablets and Effexor XR. Side effects are expected to be similar as well as demonstrated in completed [inaudible] studies.

To summarize, Venlafaxine extended release tablets offer the following: smaller tablets compared to extended release capsules, decreased pill burden at the 225 mg strength, one tablet versus two or three capsules and Meson, et al reported patients taking one tablet versus multiple tablets were more adherent to their medication regiment. Thank you for considering Venlafaxine extended release tablets.

Vyn Reese: Thank you. Are there any questions from the committee? Next up is Steven Cheng. On deck is Jake Knee.

Steven Cheng: Good morning members of the P&T. My name is Steven Cheng. I'm with Eli Lilly's Global Health Outcomes Division. Cymbalta is a selective serotonin norepinephrine reuptake inhibitor or SNRI currently approved by the FDA for four indications for adults in the acute maintenance treatment of major depressive disorder, the acute maintenance treatment of generalized anxiety disorder. This maintenance indication for GAD was announced this past month in November for the management of diabetic peripheral neuropathic pain and for the management of fibromyalgia.

Regarding major depressive disorder in a meta-analysis of six placebo and active comparator controlled clinical trials comparing the remission rates by HAM D17 scores. In patients receiving Cymbalta SSRIs or placebo patients taking Cymbalta or SSRIs had significantly higher remission rates compared with placebo. The difference between Cymbalta and SSRIs was not statistically significant. In a secondary analysis the pooled Cymbalta groups showed greater remission rates than pooled SSRI groups among patients with more severe depression, but it did not differ in patients with less severe depression. Also, two recent Cymbalta pharmacoeconomic analysis have been presented specifically for diabetic peripheral neuropathic pain. A retrospective commercially insured database analysis compared the use of opioids among DPNP patients who were given Cymbalta versus standard of care treatments.

Cymbalta treatment significantly delayed the use of opioids and Cymbalta treated patients has significantly lower total health care costs than standard of care patients over a 12-month follow-up period primarily due to lower outpatient costs. For fibromyalgia in an analysis compared Lyrica to Cymbalta and Cymbalta demonstrated significantly higher medication compliance and significantly lower total health care costs. The average daily dose for Cymbalta was relatively stable over time while Lyrica patients showed dose escalation over the 12-month follow-up period.

I would also like to briefly summarize Cymbalta's fibromyalgia efficacy data. Cymbalta 60 mg once daily has demonstrated efficacy in two randomized double blind placebo-controlled studies involving patients with fibromyalgia with or without major depressive disorder. Pain reduction was observed in patients both with and without comorbid MDD; however, the degree of pain reduction may be greater in patients with comorbid MDD. Cymbalta carries an antidepressant box warning for

increased risk of suicidality in children, adolescents and young adults and Cymbalta is not approved for use in patients under the age of 18.

I would like to respectfully ask that the P&T Committee consider adding Cymbalta to the preferred drug list based upon its broad spectrum of FDA approved indications across the multiple disease states of MDD, GAD, DPNP and fibromyalgia and proven safety in tolerability profile. Full prescribing information can be provided upon your request. Thank you very much.

Vyn Reese: Thank you. Any questions from the committee? We'll go on to the next stakeholder, Jake Knee.

Jake Knee: Ladies and gentleman of the committee, thanks for the time. My name is Jake Knee. I'm a Regional Account Manager with Forest Laboratories speaking today on behalf of Lexapro. Lexapro has recently been indicated for the treatment of adolescent depression. The Emsle(?) clinical trial was referenced in this scan so I won't go into too much detail. You can read the reference as you wish, but one of the things that is of interesting note is that this is only the second agent approved for adolescent depression. All the second generation antidepressants have, at one time or another, done the clinical trials for adolescent depression. Paroxetine for example had four clinical trials and failed all four trials. To date only Fluoxetine and Lexapro have the indication for adolescent depression.

Two interesting trials; one of which is referenced in the scan is the Cipriani trial that was recently published in the Lancet. It was a meta-analysis looking at 117 clinical trials worldwide with 12 new generation antidepressants encompassing 26,000 patients. I'd like to read you an excerpt that is in the scan but it says that, "Clinically important differences do exist between antidepressants in both efficacy and acceptability in favor of escitalopram and sertraline. Obviously this is not the time or place to talk about cost analysis but I can tell you that there's only a year and a half left, roughly, on Lexapro's patent and I can assure you that Forest is still offering the supplemental rebates, which would ensure a situation where the state would be in the black. I know that there is a legislative initiative to go for generics first. However, adding a medication to the formulary that has the adolescent indication in addition to this new evidence showing that Lexapro has a clinical rational, upwards of 30 clinical trials, 17 of which are head-to-head establishing Lexapro's

efficacy and safety. I would just like to say that we would still like the opportunity to provide this medication to the members of the state in an unrestricted fashion. If there's any way to at least put the idea in your head at least just for the adolescent patients I believe there's an EPA code that could be used for the adolescent patients so they wouldn't have to step through a non-FDA approved medication and be able to get Lexapro's access that way. So, thank you for your time very much and I appreciate it.

Vyn Reese: Thank you. Questions from the committee? Okay. I'd like to open it up now for discussion.

Jeff Graham: Vyn, this is Jeff Graham. Megan, isn't this class going to be fully updated in the next year?

Megan van Noord: Sorry. I'm having trouble hearing. What was the question?

Jeff Graham: I think this class is going to have a full update in the next year. I want to just give that information to our committee.

Megan van Noord: Okay.

Jeff Graham: That's correct?

Megan van Noord: Yes, it is.

Jeff Graham: Okay.

Megan van Noord: It was approved at the Oregon meeting.

Vyn Reese: Okay. Is there any discussion about the scan? Does anyone want to offer up a motion? The previous motion is at the end of your handout. The only difference that…is that desvenlafaxine would be on the new one.

Barak Gaster: This is Barak Gaster. Can anyone enlighten me as to why we have, on our motion, that one of the agents must be fluoxetine?

Jason Iltz: This is Jason. I believe we were covering the adolescent population with that portion of the motion.

Patti Varley: That's correct.

Vyn Reese: That's right. That's the way I remember it as well. Does anybody want to step up and…we can actually just say that the previous motion is acceptable. Desvenlafaxine I think was even on the previous drugs reviewed.

Jeff Graham: Vyn, this is Jeff Graham. No, it was not included.

Vyn Reese: We can add it under the list there just under Venlafaxine because it was reviewed this time. That's the only change that I can see that needs to be added.

Jeff Graham: Vyn, I think technically it was not fully reviewed in the scan. It's mentioned. Megan, can you give this…in the scan was it included?

Megan van Noord: It was…I didn't work on that report but my understanding it was added as an addendum because it was approved during the process. So it wasn't included at the beginning of the search.

Jeff Graham: Right. The way it was done in the update was that it was mentioned that there were two…I think it said two placebo-controlled trials with that drug and that was…there were no head-to-head trials.

Vyn Reese: It was in the abstracts that we were asked to review. There were trials with desvenlafaxine and it was…it had positive studies against placebo and it is FDA approved. It should be on the list. It was in that, you know, the abstract section.

Duane Thurman: This is Duane Thurman. I think that it is within the committee's discretion to consider this as part of the update or to say we want to wait until the full update coming. But if you're comfortable with what's presented I think it's within your discretion to include it.

Vyn Reese: They're positive studies against the placebo and they were mentioned so I think we have to include it and that would be my take on it. But I'll listen to other…

Duane Thurman: Yeah. I'm saying…I believe you have the discretion to do what you want on that.

Janet Kelly: This is Janet Kelly. Um, I'm a little uncomfortable. I didn't see any data other than the fact that it said it's FDA approved. I think in the past we've seen actual data that show that and we could review what those findings were. This is just saying that it has…

Vyn Reese: Well, in the full report that we had…not just this very brief slide presentation. There were…as I recall there was at least an abstract of studies saying that it was a…positive studies against placebo. I'm pretty sure that's correct. We only saw the abstract though, but it's been FDA approved for that. We only saw the abstract. If you want to say not to approve it until we read the whole paper that's fine too. But it is FDA approved. There are abstracts that we reviewed that were positive that have been published, I believe.

Carol Cordy: This is Carol Cordy. Somebody give me the practical interpretation of this. If someone were to prescribe desvenlafaxine what would happen if we don't include it in this?

Siri Childs: For Medicaid…this is Siri Childs and for Medicaid what would happen is that they must have tried and failed at least two preferred drugs before they could have Prestiq and it would not be subject to TIP or to DAW because it's considered not studied.

Carol Cordy: Okay. So if we leave this as is and don't add it until we get the full review that's what would happen?

Siri Childs: Right.

Carol Cordy: If we add it…

Siri Childs: Medicaid would treat it as…well, we would have to do the cost analysis and do the comparative cost analysis and then, because it's part of the PDL it would be subject to TIP and DAW.

Carol Cordy: Okay.

Siri Childs: It also, eventually through the next year would be subject to our generics first initiative.

Barak Gaster: This is Barak Gaster. But this class is not subject to TIP.

Carol Cordy: Yeah it is.

Barak Gaster: Our last motion said that it didn't…that it cannot be subject to TIP.

Siri Childs: Sorry, my mistake.

Duane Thurman: This is Duane Thurman again. I want to make it clear that this staff is not making a recommendation one way or the other. I think what you need to do is look at what was presented, question the presenter and based on the evidence you've heard make a decision as to whether you believe you want to include it or not. The effect of including it would simply put it into the pool of the other drugs and then we would do our cost analysis to come out with the preferred drugs and then as Siri pointed out once the generic first kicks in then that will be a threshold issue. You start with the generic and then work your way into our preferred drug list.

Patti Varley: This is Patti Varley. Question, when would that full review be done? Do we have a date?

Jeff Graham: Well, we try to schedule these on a yearly basis so it would be ready for us to look at in December of 2010. If it is released in August we might look at it in October, but I don't think it would be ready before August.

Vyn Reese: Any further discussion? Do we want to include Prestiq as a drug on the list or do we want to not to delete it? It's got positive studies. It's been approved by the FDA. It's hard to imagine not having it on the list and it's also an isomer of one of the drugs on the list. So it's hard to imagine not…I doubt it's going to be on the preferred drug list given that it's a new drug…other than…it's not going to be one of the preferred drugs and it's not a generic.

Barak Gaster: This is Barak Gaster. I would suggest that we have it on the list.

Vyn Reese: Any discussion on that?

Jason Iltz: This is Jason. Um, you know, the data that we have is only abstract and it's small numbers of people, open label studies, you know, placebo-controlled. So I don't know that we've ever considered it with that little

of evidence before, especially from a scan standpoint where there was really nothing mentioned other than there were some studies. So I guess my take would be that I think it behooves us to wait until the full update and make a motion that is reflective of the body of evidence that we have for all of the other medications.

Vyn Reese: We can have a vote to deny it or to put it on the list. That might be a way to manage this if there is dissent in the committee. So…and I can just basically say how many of the committee would support putting Prestiq or desvenlafaxine on the preferred drug list? All those in favor say, "Aye".

Group: Aye.

Vyn Reese: And opposed, same sign?

Group: Aye.

Vyn Reese: So Prestiq is not on the list. Now can we…

Jason Iltz: I can take a stab at the motion. And I'll just…I don't really see…I guess we can have a discussion as to…we're still okay with fluoxetine and naming certain ones to make sure we're covering the different mechanisms and classes. Is that an okay assumption?

Patti Varley: This is Patti. Whether you name a particular agent or not I think clearly identifying that an approved medication within the pediatric population needs to be included. So I would…that amending would be fine by me as opposed to a specific medication, but I think there needs to clearly be the identification of agents that have been approved for use in the pediatric and adolescent population.

Jason Iltz: So if we…let me just start here and take a stab at this. After considering the evidence of safety, efficacy and special populations for the treatment of major depressive disorder, I move that bupropion, citalopram, duloxetine, escitalopram, fluoxetine, sertraline, fluvoxamine, mirtazapine, paroxetine and venlafaxine are safe and efficacious. The Washington Preferred Drug List must include at least two SSRIs one of which has an indication for pediatric and adolescent use, at least one SNRI, mirtazapine and bupropion. The second generation antidepressants cannot be subject to therapeutic interchange in the Washington Preferred Drug List.

Vyn Reese: Is there a second?

Barak Gaster: This is Barak Gaster. I second the motion.

Vyn Reese: All those in favor say, "Aye".

Group: Aye.

Vyn Reese: Opposed, same sign. The motion's passed. Let's move on to the next…

Jeff Graham: Megan, I think you could probably leave now.

Megan von Noord: Okay. Thank you. Bye.

Jeff Graham: Thanks a lot. And is Kim Peterson on the line? She should be shortly. Kim, are you on the line? Hmm. Kim, is that you?

Kim Peterson: Yes.

Jeff Graham: Good. We're ready for you and your slides are up.

Kim Peterson: Okay. You have the slides up?

Vyn Reese: Yeah, the first slide is up. Why don't you go ahead? This is Dr. Reese.

Kim Peterson: Okay. So the first presentation is on the fourth update of the beta blocker review.

Jeff Graham: That's correct.

Kim Peterson: Okay. Let's go ahead and go onto slide number 2 then. So I'll start with a quick review of the inclusion criteria. In update four there were no changes to the included populations and those are listed on the slide there. So the reviews focused on use of beta blockers in adults for treatment of hypertension, angina, status post coronary artery bypass graft, recent myocardial infarction, heart failure, atrial arrhythmias, bleeding esophageal varices and for migraine prophylaxis. There's a few caveats. For angina we only included studies with durations of two months or longer. For coronary artery bypass graft patients we only included studies

of long-term treatment and included…and excluded studies of the short-term use of beta blockers just to suppress atrial arrhythmias. And then for recent MI or heart failure we only included studies with sample sizes of 100 patients or more.

Let's go on to slide number 3. Here's a list of included drugs. For this update we added nebivolol which received FDA approval for treatment of hypertension on December 17th of 2007. Next slide.

Here's an overview of the sources of new evidence that we reviewed for this update. We updated our searches of the usual electronic databases going back to March of 2007, which was the cutoff date from the previous update and the search end date for this update was February of 2009. Also for this update we received new dossier submissions from the manufacturer's of carvedilol, carvedilol controlled release and nebivolol. Next slide.

This is an overview of the included studies overall with the numbers in parentheses specifically representing the numbers of new studies we added for this update. This is a pretty small update with only nine new trials and the majority of those involved nebivolol. Four were head-to-head comparisons of nebivolol to other beta blockers and two were placebo-controlled trials of nebivolol. Next slide.

So now on to the results, which will be presented by population starting with hypertension. So for this update we added two new trials and both were head-to-head trials of nebivolol compared with metoprolol. One trial randomized 48 men to either nebivolol 5 mg once daily or metoprolol succinate 95 mg once daily and measured erectile function after 12 weeks. And the other randomized 46 men and women to receive open treatment with either nebivolol and a median dose of 5 mg once daily or metoprolol at a median dose of 100 mg. That trial measured impact on sleep after six weeks. So these were both pretty small and short-term trials and neither found any significant difference between nebivolol and metoprolol on either outcome and neither reported adverse events. So evidence from this update did not result in any changes to our previous conclusions about direct comparisons between beta blockers. That (1) we haven't found any head-to-head trials that directly compared different beta blockers for long-term health or quality of life outcomes and (2) in the shorter term trials there have been no consistent differences between beta blockers and

quality of life related outcomes. And three head-to-head trials have not found any consistent differences between beta blockers and harms. Go on to the next slide.

For the treatment of angina and for this update we only added one new trial. It was a head-to-head trial that compared betaxolol 20 mg once daily versus metoprolol 50 mg twice daily in 112 adults for eight weeks. And the primary outcome measure was compliance and then secondary outcomes included quality of life and angina attack frequency. There were no significant differences between betaxolol and metoprolol found on any of those outcomes and harms were not reported. So again evidence from this evidence did not result in any changes to our previous conclusions about direct comparisons between beta blockers that there are no consistent differences in effectiveness and efficacy outcomes in adults with angina. And then for harms although there was a great incidence of overall adverse events for propranolol compared with pindolol in one trial this finding hasn't been replicated and there were no significant differences in overall adverse events in any other head-to-head trials of beta blockers. Next slide.

So now on to results in trials of beta blockers used following coronary artery bypass graft. And we added no new trials in this population for this update. So there were no changes to our previous conclusions. That there is only limited evidence from two placebo-controlled trials of metoprolol tartrate and it doesn't support a benefit of beta blockers…or on mortality or ischemic events in this population. Next slide.

For treatment following myocardial infarction…and for this update we added one trial that compared carvedilol 12.5 mg twice daily to metoprolol tartrate 100 mg twice daily. In 113 high-risk adults with left ventricular dysfunction after acute myocardial infarction and after a mean follow-up period of 13.4 months no significant differences were found in the primary end point of time to the first cardiac event, which included all cause mortality, re-hospitalization for a cardiovascular event, revascularization with percutaneous coronary intervention or bypass surgery, post infarction angina pectoris with documented electrocardiographic signs of ischemia and heart failure requiring additional treatment with digitalis diuretics or inotropic agents. So all those events I just listed off were what was included in that composite primary end point and there were no significant differences between carvedilol and metoprolol and harms were not

reported in this trial. And so again evidence from this update did not result in any changes to our previous conclusions that head-to-head trials have not found any consistent significant differences between beta blockers in adults following myocardial infarction and harms have not yet been reported in any head-to-head trials. Next slide.

And then in this slide we have a summary of evidence from placebo-controlled trials of beta blockers used in adults post myocardial infarction and there were no new trials added for this update. So there were no changes to our previous conclusions that acebutolol, metoprolol tartrate propranolol and timolol have all shown similar mortality benefits relative to placebo in post myocardial infarction patients without other complications. And then based on the big CAPRICORN trial carvedilol is still the only beta blocker shown to reduce mortality compared to placebo and post myocardial infarction patients who have asymptomatic or mildly symptomatic left ventricular dysfunction as demonstrated by an ejection fraction of less than 40% and who are already taking an ace inhibitor. Next slide.

Okay. Now on to evidence from the head-to-head trials of beta blockers and heart failure. We added one trial for this update. This was a trial that involved 70 adults aged 35 years or older with a left ventricular injection fraction of over 40%...I'm sorry, a 40% or below and a New York Heart Association functional class of two or three who were randomized to six months of open label treatment with either carvedilol 25 mg twice daily or nebivolol 5 mg once daily. And results found no significant differences between carvedilol and nebivolol in improvement of New York Heart Association functional class or on a six-minute walk test distance. Also no significant differences were found in overall adverse events, [inaudible], hypotension or withdrawals due to adverse events. So again evidence from this update did not result in any changes to our previous conclusions that head-to-head trials have not found any consistent significant differences between beta blockers in symptom related outcomes and the only difference in harms was the higher rate of dizziness for carvedilol compared with metoprolol tartrate in one trial. Next slide.

Vyn Reese: I had a question about that last one.

Kim Peterson: Sure.

Vyn Reese: On harms did they mention postural blood pressure changes or just the complaint of dizziness?

Kim Peterson: I didn't hear the last part of your question. Did they mention postural blood pressure or…and then I didn't hear.

Vyn Reese: Possible blood pressure changes was that also measured? I mean dizziness often reflects postural blood pressure drops. Was that one of the things they looked at in that study or not?

Kim Peterson: Oh. You know, we didn't look at that as an adverse event outcome so I can't say if they measured it or not although if…when we get to…when we get to the end of the presentation while the public comment is happening I can look up that study and find that information for you.

Vyn Reese: Great. Thank you.

Kim Peterson: Okay. So postural blood pressure changes. Okay. Again, the evidence from this new head-to-head trial didn't result in any changes to our previous conclusions, that so far head-to-head trials haven't found any significant differences between beta blockers in the symptom related outcomes or in harms except for just in one trial. So let's go on to the next slide where we're looking at the larger placebo-controlled trials that measure…that were longer term and measured the longer term health outcomes. For this update we added one trial of nebivolol and it was a very large trial that randomized over 2,000 patients from multiple sites across various Western and Eastern European countries. The acronym for this trial is SENIORS, which standards Study of the Effects of Nibivolol Intervention on Outcomes and Re-Hospitalization in Seniors with Heart Failure. And so by the name you can guess that it specifically targeted patients who were older and it also targeted patients who were a little healthier than in the prior major trials. So in SENIORS the mean age was 76 years and the mean ejection fraction was 36% as compared with 20 to 28% in the previous trials and the mean annual placebo group mortality rate, which was 10% was lower than compared to the previous major trials in which it ranged from 11% to 19%. And as for the results their primary outcome was a composite measure of all cause mortality plus cardiovascular hospital admission and on that primary outcome measure nebivolol was found superior to placebo. The hazard ratio was .86 and the 95% confidence interval was .74 to .99. However, when the components

of the primary outcome were examined individually as secondary outcome measures differences between nebivolol and placebo were not statistically significant. So just when you look at all cause mortality alone there was no significant differences between nebivolol and placebo. Next slide.

So here's the evidence from placebo-controlled trials that focused specifically on patients with severe heart failure and there was no new evidence for this population for this update. There was no changes to report to our previous conclusion that carvedilol is still the beta blocker that has the strongest evidence of reducing mortality in this population. Next slide.

Okay. So now on to the evidence from trials of atrial arrhythmia and there were no new trials added for this update. So there's no changes to our previous conclusions as outlined in this slide, that there are no significant differences between bisoprolol and carvedilol in atrial fibrillation relapse prevention or for withdrawals due to adverse events in the only head-to-head trial that we found to date. So there's more evidence from placebo-controlled trials showing that atenolol, nadolol, pindolol and carvedilol all have been found superior to placebo in improving ventricular rate control whereas labetalol offered no significant benefit over placebo on that outcome. And only metoprolol succinate has been found to be superior to placebo in atrial fibrillation and flutter relapse prevention and then only carvedilol has been found to be superior to placebo in improving rate control and functional capacity in adults with atrial arrhythmia and comorbid heart failure. Next slide.

Okay. So now on to evidence from trials of meta blockers for migraine prophylaxis and for this update we added one trial that randomized 30 adults to double blind treat…with either up to 142.5 mg of metoprolol or up to 5 mg of nebivolol for 18 weeks and the results of this trial found no significant differences between nebivolol and metoprolol and decreases in angina…in attack frequency…I'm sorry, in migraine attack frequency, severity, number of headache days and number of tablets of acute drug treatments consumed. But rates of overall adverse events bradycardia and hypotension were lower for nebivolol. So as for our overall conclusions other than the tolerability advantage of nebivolol or metoprolol in the new trial head-to-head trials have not found any consistent significant differences between beta blockers in effectiveness, efficacy or harms outcomes. Next slide.

For the treatment of bleeding esophageal varices...and for this update we found no new trials. So there's no new changes to our previous conclusions. We only have limited evidence from one head-to-head trial of atenolol compared with propranolol and that found no significant differences between those two beta blockers and then from placebo-controlled trials they do not suggest any consistent differences between beta blockers and effectiveness, efficacy or harms. Next slide.

Here's a summary of the comparative evidence for beta blockers in subgroups and we found no new comparative evidence for this update. So there was no change to our previous conclusion. As we stated here that no beta blocker has been found to be more effective or associated with fewer harms than any other…in any subgroups of patients based on age, racial groups, gender, other medications or comorbidities. So next slide, which is the last slide.

So just to wrap things up as I mentioned the main findings from this update related to nebivolol, which was the new drug added for this update. So it has FDA approval for hypertension. We added two trials in hypertension both finding no significant differences compared to metoprolol on erectile function and sleep. One trial in heart failure finding no significant differences versus carvedilol in the symptom related outcomes but was superior to placebo in the older population on that composite outcome of mortality and re-hospitalizations and then finally evidence in migraine…for migraine prophylaxis that it had similar effects to metoprolol. So that was the kind of bottom line of this update with the evidence for nebivolol.

So I'll go ahead and turn it back over to you for other questions.

Vyn Reese: Thank you. Any questions from the committee? Can you just remain on the line, Kim, until the stakeholders finish speaking? The first stakeholder is Mr. Jake Knee. On deck is Long Nguyen.

Jake Knee: Hello again. Um, as you can guess I'm here today to speak about Bystolic or nebivolol, the newest entrance in the beta blocker market. Um, there are some interesting characteristics of Bystolic that I think you all will find interesting. This is a fourth generation beta blocker. It is also the only beta blocker that is both cardio selective to beta 1, but also vasodilating. It

is roughly anywhere from 7 to 10 times more selective to beta 1 versus beta 2 than the next most selective beta blocker, which happens to be metoprolol. It also has a secondary mechanism of action which is nitric oxide mediated vasodilatation in the endothelium. So amongst vasodilating and hypertensives it has some unique characteristics. Obviously because it vasodilates in the endothelium both the vascular and the arterial you don't have some of the side effects associated with classic beta blockers and/or vasodilators. So for example first the calcium channel blocker it's not associated with peripheral edema. You don't get a lot of the orthostatic hypotension associated with some of the other vasodilators. And interestingly if you look at the hemodynamic profile of nebivolol it also doesn't quite fit up with what a classic beta blocker would look like.

Historically, beta blockers they have their mechanism of reducing blood pressure by reducing cardiac output or reducing heart rate. This medication also reduces heart rate, but maintains cardiac output and in most hemodynamic trials actually had a slight bump numerically. So what that says is there's something else going on. It's that vasodilatation that decreases peripheral vascular resistance. Classic beta blockers increase peripheral vascular resistance. So what you end up having is those side effect advantages. When you maintain cardiac output you typically don't get exercise intolerance, sexual dysfunction, cold extremities. This drug is not contracting the vascular like classic beta blockers do. So it's a very efficacious medication. A trial that was published in the American Journal of Hypertension by the Corse showed in combination with hydrochlorothiazide you can get with 10 mg of nebivolol with 25 mg of hydrochlorothiazide, 29 over 15 ml drops with placebo like side effects. So you get, interestingly enough, also some very good efficacy due to that secondary mechanism in the special populations. This drug has been specifically studied in the elderly as well as African Americans and for [inaudible] deficient patients or volume dependent hypertensive patients this drug works equally as well in those populations as it does the general population. So for those special populations that typically don't get efficacy from a beta blocker or can't tolerate it nebivolol has been shown to work very well in those populations and the general [inaudible] profile is something you'll certainly not see from any other beta blocker.

So having said that and in closing I would like to also mention that Forest did a very strange thing in bringing a brand new drug to market pricing it below…

Jeff Graham: Please conclude your remarks.

Jake Knee: Certainly. Pricing it below metoprolol ER which is a generic. So I think you'll be surprised if you give this drug open access to state will in fact not have any more expenses than they would per se of metoprolol ER. So, thank you for your time.

Duane Thurman: Excuse me. This is Duane Thurman. I just want to point out that testimony with regard to cost, cost analysis and all of that is not appropriate before the committee. Please stick to the evidence based comments about your drugs.

Jake Knee: I apologize.

Vyn Reese: Any questions from the committee? The next stakeholder is Long Nguyen from GSK.

Long Nguyen: Good morning. My name is Long Nguyen, PharmD, Regional Medical Scientist for GlaxoSmithKline and I'm here to represent…share with you…any questions that the committee may have on Coreg and Coreg CR and I understand that during the presentation there was a question from the committee member in regards to the…one of the trial that looked at carvedilol and noted that the carvedilol group actually have a higher incidence of dizziness and the question from the committee member was that was orthostatic hypotension measured in that trial and in that particular trial orthostatic hypotension was not…is not an end point or a measurement in that trial. They were just looking at the report incidence from the patient's subjective whether they felt dizziness or not during the trial.

In regard to that if you remember when carvedilol was approved in early 1993 there was a statement in carvedilol PI that request any patient start on new therapy they need to be monitored for the first two hours to ensure that there's no orthostatic hypotension and because none of this…there's no increased risk of orthostatic hypotension seen in this…in the post marketing experience there was a change in the PI that do not require

patients to be monitored and that's why it's no longer a measurement in any of our trials including the comment trials. So I hope I was able to address that question for the committee member and with that one of the differences between carvedilol is it is a vasodilating beta blocker but the mechanism is not nitric oxide, but it's an alpha one blocker. And it's a completely different mechanism so I want to differentiate that alone other beta blockers available out there for the patient. And with that I'll be happy to entertain any questions the committee…committee member may have.

Vyn Reese: Thank you. Any questions from the committee? Okay. Thank you.

Long Nguyen: Thank you very much.

Vyn Reese: I'd like to open it up for discussion. This is a full update.

Barak Gaster: This is Barak Gaster and one of the things that I'm noticing is that the motions for each of the indications include that the list of drugs can be subject to therapeutic interchange for that indication except there's no statement in the congestive heart failure motion as to whether the drugs can or cannot be subject to interchange. I guess I'm wondering if we would want to make a distinction for that indication that they may not be subject to interchange because of the difference in level of evidence for carvedilol. Although it's gotta be difficult from the level of the pharmacy to figure out what the indication is for a given prescription.

Vyn Reese: Right, that's the problem.

Barak Gaster: And so I guess…

Vyn Reese: Carvedilol is approved for stage 4 heart failure and hypertension and metoprolol succinate is approved for…they're both generics now too. That's the other complicated thing.

Barak Gaster: I'm just noticing that we should probably address that issue.

Vyn Reese: Any other additional discussion?

Carol Cordy: This is Carol Cordy. I'm assuming that because it does not state that they can be…we're just assuming that they can't be. Is that what the…for the

congestive heart failure? I don't remember but was that our intention that by leaving that they can be subject to therapeutic interchange implies that they cannot be? How would that be interpreted?

Jason Iltz: This is Jason. You know, the PDL itself doesn't list these as subclasses of indications as we have them here and from a motion standpoint. So I think the class itself, if I go back to the PDL it is subject to therapeutic interchange if I read it correctly. Is that…am I interpreting it correctly? Again, at the pharmacy level we don't often see on the prescription itself what the indication is but a lot of times when you get to know your patients and you can look at the rest of their profile it's pretty indicative as to why they may be taking it although there are some patients who take carvedilol for both hypertension and for a congestive failure. So there's some issues there. I don't know that…I think it's working from a standpoint of this class in general makes sense to have therapeutic interchange with all the different generics and, you know, I think it just continues to make sense, but I certainly would entertain other discussion if we're worried about that specific indication for one reason or another.

Patti Varley: This is Patti Varley and I guess I'm…I can't remember our discussion about that in the past and I…but I do recall that in other circumstances when we feel strongly there should not be that we include a statement saying "should not be subject to" and this one is lacking both. So I, you know, unless someone remembers something I don't I don't remember the specifics as to why that was or was not left out in that particular category.

Duane Thurman: This is Duane Thurman. I think you're correct that normally you would say, "Yes or no". My vague recollection about this, and I need help from Siri and Jaymie is that the effect of congestive heart failure sub motion was basically to say you have to have one of these, one or the other, and so there was no issue as to therapeutic interchange. That you would say you need these two drugs and that we will do our cost analyses and it ensures that at least one of those drugs was on. So I don't think you made any statement about interchange because there was no need to.

Vyn Reese: It sounds like too though that we had both of them on the preferred drug list for heart failure. So like if we have both of them on the list you can't interchange them. It's a moot point.

Siri Childs: Yes.

Vyn Reese: For that very reason because it's hard to know what stage of heart failure you're in.

Patti Varley: This is Patti again. I'm just…out of curiosity since…is there a rationale or a safety issue about categorizing these by diagnosis as opposed to talking to them about a group as a whole? Especially in regard to the fact that I do believe that it is rare for the pharmacy to be given a prescription that has "for migraine headache", "for hypertension", "for congestive heart failure". Now I could be wrong, but I'm curious as we're talking today about these things. Is there a need for these to be separate motions or is it a class motion that we could group together?

Vyn Reese: This is Dr. Reese. As I remember it we broke it down like this because they are FDA approved for different indications. We also could just put them on…all the indications down and then we could list all the beta blockers and just say, "These are under PDL for the indications they're approved for." I mean that's another way of managing this massive drug class with all these uses and indications. So I mean we could look at just combining all of those into one large motion and that might be a better way to look at it just for the ones they're approved for and we can say the drugs that we really want to have on the…that we want to make sure that are on the PDL like we did before for drugs that have been approved for certain indications like heart failure where none of the other drugs are approved. We probably need both carvedilol and metoprolol succinate; they need to both be there. That's the only one I can think of where there's gradations of…when one drug is approved at a certain level and the other one hasn't gotten approval at that level where there's gradations in illness.

Siri Childs: This is Siri Childs and the first time that you did the review of this drug class the three agencies did put a matrix together listing all of the drugs by their indication and then it was quite easy for us to make sure that we included every single drug as a preferred agent that was in one of those classes. And so we've been doing that for several years and I think that we've been pretty successful at, you know, providing all of the drugs and now almost all of them are generic and represent each of the indications. So it becomes even more easy as we go along. We did have carvedilol on EPA for a special population that as soon as it became generic and could

go full review…or full preferred we moved it to preferred without any restrictions at all.

Vyn Reese: So would that be an easier way to manage it just if we basically listed all of these drugs, all of the diseases and just say the drugs that are FDA approved for these indications should be on the list and that carvedilol obviously has to be on the list.

Siri Childs: I don't think that you need to change your motion at all. Your motion gives us the direction that we need to make sure that there's a drug in each of the categories for the FDA labeling.

Vyn Reese: Right now it's we have one for every single indication. We list them all and then we have the drugs that are approved for those indications. That's a very cumbersome way to do it, as been mentioned earlier. I'm wondering if we should just try and lump them together and make one large motion.

Duane Thurman: This is Duane Thurman. I just want to make a suggestion that…I guess the point is this has been working well for us for three years and if you want to do a cleanup motion like that it might be better when we have a substantial change to the drug class because it's more likely we'll pick up a mistake or something if we try to re-write what's been working.

Vyn Reese: Okay.

Duane Thurman: That would be my recommendation.

Vyn Reese: And as I understand it the only drug to be added is nebivolol and that's just for hypertension.

Duane Thurman: I'm sorry.

Vyn Reese: What else was it approved for? What is it FDA approved for? I think it's hypertension. What is it…the way I remember it, it only has a couple of indications. I don't think it has the congestive heart failure indication yet.

Barak Gaster: Barak Gaster. We looked at data using nebivolol for congestive heart failure, for hypertension and for migraine.

Vyn Reese: But the data on congestive heart failure was confusing. It's not superior to placebo.

Barak Gaster: For that outcome of mortality in a healthy population.

Vyn Reese: Yeah. I don't think it has that indication yet. I'm looking here in my Palm and it says hypertension. I don't have the full review with me. I think it had only one or two indications.

Siri Childs: This is Siri Childs again. I guess the key to the new drug is, "Does it have an indication that no other drug has?"

Vyn Reese: It doesn't.

Siri Childs: Okay.

Patti Varley: This is Patti Varley again. I think the question was regardless of that do we need to list it as we have listed it? And if so, where? And I think what everybody is saying is that right now the only FDA indication is hypertension or somebody is checking on that for sure and if so that's where it should be listed. Is that correct?

Vyn Reese: It has to be on…I mean we can't limit this list. The drugs that are FDA approved and we've actually reviewed two and it's like…I think we're going to be too limiting. So we need to make sure that it's on the list. It's not going to be an approved drug because it's new and it's not a generic given the generic first. But it needs to be on the list for the areas where it's FDA approved. Has anybody looked that up to make sure it's…is there any other indication it has other than hypertension?

Duane Thurman: I have not.

Siri Childs: Could we ask our stakeholder?

Woman: Is it systolic? Is that what you're asking?

Vyn Reese: Yeah, exactly.

Woman: Hang on.

Man: It's just indicated for hypertension.

Vyn Reese: Yeah, that's what I have. That's the only place it should be on the list.

Alvin Goo: This is Alvin. But at the same time with CHF bisoprolol also does not carry that FDA indication although there are studies to suggest that it would be beneficial in heart failure. So I just want to caution and I don't think we want to just be restricted to FDA approved indications. I think if there's evidence of a drug that it's beneficial and there's strong randomized trials indicating benefit, you know, it might not have FDA approval. So I just want to caution that we…I just want to be careful that we don't want to restrict ourselves just to FDA indications.

Vyn Reese: I think doctors are commonly doing…ordering drugs for off label use that have good evidence. So it's not an uncommon thing you do that. But I'm not sure we have to…but if there's no good evidence right now to see that it has approval for heart failure…I don't see any persuasive evidence.

Duane Thurman: This is Duane. I think that you…in the sense of us building our preferred drug list we do have to respect the FDA indication and I think that the problem or the issue that you raise is something that you deal with through "dispense as written" or the clinical decisions of the dispenser.

Patti Varley: Right. This is Patti Varley again. I mean what we're trying to do is to have them start with the safe and efficacious medications that have been approved for those uses. Clearly there's no restriction that if someone has tried on those and is unsuccessful and needs to move to something alternative that has evidence, um, they would not be stopped from doing that, but on the other hand what we're talking about is the initial decision making should follow the logic of safety and efficacy and FDA approval initially.

Duane Thurman: Right. I'm saying for the purposes of our PDL we would not have a non-FDA approved drug as preferred for a particular indication if it wasn't approved.

Vyn Reese: Exactly.

Patti Varley: Right. Exactly.

Vyn Reese: Okay. Does somebody want to start through this gigantic list of motions or are we at that point yet?

Carol Cordy: This is Carol Cordy. I'm just wondering if other than the nebivolol if Alvin's motion here…I move to accept and continue the previous motions for the beta blockers with that one exception of adding nebivolol to the hypertensive list. We could not have to read through every single one.

Duane Thurman: Yeah, this is Duane. Sorry to be Chatty Kathy, but I think you're right. I don't think we need to stick to the, you know, we don't have to re-read these each time and I think you can say that you reiterate the prior motions except for X and even at that point instead of re-reading the whole motion you could say, "We accept the motion in its terms, but add a particular drug."

Vyn Reese: Is the committee in agreement with that?

Patti Varley: Yes.

Man: Yes.

Vyn Reese: It sounds easier. So do you want to start…do you want to make your motion…Alvin, did you make that motion? Do you want to make it an official motion and we'll add nebivolol to hypertension and then…

Alvin Goo: As being reviewed under the…

Vyn Reese: As being reviewed…

Alvin Goo: Okay. This is Alvin. I move to accept the…to accept and continue the previous motions for beta blockers in addition to adding nebivolol for the indication of hypertension.

Vyn Reese: Any further discussion?

Jason Iltz: This is Jason. So just as an amendment to be clear I think we need to say something to with the addition of adding nebivolol as a reviewed agent for the indication of hypertension…as a reviewed agent for safety and efficacy for the indication of hypertension. Because I don't think what we're saying here is that it needs to be added to the PDL. We're saying it

needs to be added to the list of medications that were reviewed as being safe and efficacious. Does that clarify it?

Patti Varley: Yes.

Jason Iltz: Is that okay, Alvin?

Alvin Goo: Sure. I accept.

Patti Varley: This is Patti Varley. With the amendment I will second that.

Vyn Reese: So it's still not amended.

Jason Iltz: So the other part of it was with the addition of adding nebivolol as a reviewed agent for safety and efficacy…

Vyn Reese: As a reviewed agent that is safe and efficacious…

Jason Iltz: Yeah, that is safe and efficacious for hypertension. Thank you. Thank you, Vyn.

Duane Thurman: For the treatment of.

Vyn Reese: Safe and efficacious.

Patti Varley: In the treatment…

Vyn Reese: For the treatment of hypertension.

Patti Varley: Oh.

Jason Iltz: So shall we read it for the minutes?

Vyn Reese: This is Alvin's motion, right?

Alvin Goo: Correct.

Vyn Reese: But you modified it and you're going to second it?

Jason Iltz: Sure, I'll second it.

Vyn Reese: Or did Patti second it?

Patti Varley: I can third it.

Alvin Goo: Okay. So this is Alvin again. I move to accept and continue with the previous motion for beta blockers with the addition of adding nebivolol for…as a reviewed agent that is safe and efficacious for the treatment of hypertension.

Jason Iltz: This is Jason. I'll second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay. It's passed. Now we have a break and…

Jeff Graham: A break until 10:30.

Vyn Reese: So 10:30.

Jeff Graham: And then Kim can come back on the line at that time. All right, Kim?

Kim Peterson: Okay. I'll call back at 10:30.

Jeff Graham: Good. Thank you.

Vyn Reese: Thank you, Kim.

Kim Peterson: Okay. Bye.

Vyn Reese: Kim, are you on the line?

Kim Peterson: Yes.

Vyn Reese: Okay. Are you ready to go? We're going to launch into hepatitis C. Could I have everybody take their seats please? Okay. The first slide on the drug class review for pegylated interferons is up.

Kim Peterson: Okay. Great.

Vyn Reese: For hepatitis C drugs.

Kim Peterson: So now I'm going to be presenting findings from the June 2009 scan of the DERP review on pegylated interferons for chronic hepatitis C. This is the second scan for consideration of the first update of this review. Next slide.

So the review was last assessed for updating in May of 2008 at which time the DERP participating organizations voted against a full update. So that means that the most recent final report is still the original report from May of 2007. Next slide.

And the next few slides list the inclusion criteria for populations, interventions and outcomes. For populations the scope was limited to non-pregnant adults with chronic hepatitis C with a number of pre-specified subgroups as listed and for interventions there's just the two pegylated interferon products both used in dual therapy with ribavirin. Next slide.

And this slide lists the effectiveness and harms outcomes. We were primarily interested in the long-term effectiveness outcomes including things like sustained virologic response, normalization of live enzyme abnormalities and so on and only included the early virologic response in head-to-head trials. And then as for harms we included the usual outcomes of overall adverse events, withdrawals due to adverse events and rates as specific as serious adverse events. Next slide.

So here's the details of the MEDLINE search that we conducted for this scan. We started the scan search from the end date of the last scan search, which was April of 2008 and the search end date for the scan was June of 2009 and we found a total of 90 new citations. Next slide.

And among the 90 new citations from the scan we found 19 potentially relevant trials. Five of those are head-to-head trials and regarding their scope whereas the original report and the previous preliminary update scan only found short-term trials of 8 to 12 weeks duration that only assessed end of treatment virologic responses. Three of the 5 head-to-head trials identified in the current scan assessed sustained virologic response over 24

to 48 weeks. And also one head-to-head trial evaluated quality of life outcomes over 48 weeks. And then as for the other 14 trials we found in the scan 13 compared different doses or durations of the same pegylated interferon and one was a trial that compared pegylated interferon to a non-pegylated interferon product that we would consider adding to…to update…to use to update the indirect comparison meta-analyses that was done in the original review. Next slide.

This slide provides a cumulative total of new relevant trials that have emerged since the original final report. So in addition to the 19 new trials we found in the June 2009 scan we had previously found 20 new trials in the first scan that we conducted in May of 2008. So now we are aware of a total of 39 new trials that would likely be added in a full update of this review. Next slide.

So now for results of the FDA website searches for new drugs, indications and safety alerts and for new drugs the only thing we found was that in June of 2008 the FDA approved a new combination pack that contains a single dose of peginterferon alfa-2b together with a single dose of ribavirin. So I think it's just more packaging. Next slide.

And then as for new indications what we found in our FDA web site search is that in December of 2008 indication for peginterferon alfa-2b given in combination with ribavirin was expanded to include the treatment of pediatric patients 3 to 17 years of age with chronic hepatitis C. So to clarify the DERP review has always been limited to the adult population and so the search results have not included studies in the pediatric population. But in hearing that the FDA has approved treatment in children we anticipated that DERP might have interest in considering expanding the scope of the review and include pediatric populations. So as part of the scans to give DERP participating organizations an idea of the potential size of the body of evidence involved in expanding the scope to include children, we did another search specifically to identify potential eligible trials in children and we really didn't find much at all. The available data was quite sparse. We found the one publication by Murray and colleagues from 2007 that described the methods and design, but not the results from one placebo-controlled trial of dual therapy with pegylated interferon alpha-2a plus ribavirin and then the only other publication we found in the pediatric population was by Wirth and colleagues from 2005 and it was an uncontrolled open label study of 62

children undergoing treatment for pegylated interferon alpha-2b plus ribavirin. So the DERP participating organizations have not yet elected to change the criteria to include children, but in the event that they did so far there wouldn't be too much evidence to add it looks like. Next slide.

On to the safety alerts. The first few pertain to the alpha-2a product and the first one is from April of 2009 and it involved the addition of serious retinal detachment to the adverse reaction section in response to post-marketing experience reports. And the second one is from December of 2008 and it's a notification that information on a risk of cerebral vascular complications due to stroke was added to patient package insert medication guide. Next slide.

And here's the last safety alert. This one pertains to the alpha-2b product and it's from May 2009. It's a notification of a broad variety of adverse events. Some of them are rare and quite serious, which were added to the adverse reaction section of the product label. Again, based on post-marketing experience of spontaneous and voluntary reports submitted to the FDA and we…but we add the caveat here that because these reactions are reported voluntarily from a population of uncertain size it's not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. And also just a note that a few of these like hearing loss and skin reactions are already noted in the 2a product label as well. Next slide.

So that was all from the FDA website searches and we didn't find anything additional on new drug indications or safety alerts from the search of the Health Canada website. That concludes this summary of the new evidence we found from the June 2009 scan of the review and based on the new evidence the DERP participating organizations again voted against the full update of this review. So the next time an update of this review will be considered will be in approximately June of 2010. So I'll turn it back over to you for questions and discussion.

Vyn Reese: Any questions from the committee? I'll take a motion to accept the scan.

Barak Gaster: This is Barak Gaster. I move to accept the scan.

Vyn Reese: I'll take a second.

Ken Wiscomb: This is Ken Wiscomb. I'll second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay. The scan is accepted. It doesn't look like there's a lot new in this area. Does anyone want to just re-make the last motion? Just a second. We do have two stakeholders. The first is Vandana Slatter from Genentech and the second is Isaac Lloyd from Merck.

Vandana Slatter: Good morning. My name is Vandana Slatter, Medical Liaison Genentech, a member of the Roche Group. Thank you for the opportunity to provide a clinical update of peginterferon Pegasys alpha-2a in patients with chronic viral hepatitis. Three out of every four hepatitis C patients are on Pegasys. Clinical data over 3,500 patients have been published in the New England Journal of Medicine including eight pivotal trials supporting the label and several recent trials. All future regiments of new direct anti-viral agents, DAAs that are being developed are being developed with Pegasys as the backbone long-acting interferon. The FDA has approved chronic indications of hepatitis unique to Pegasys in combination with ribavirin or alone treatment of patients with compensated HCV cirrhosis coinfected with HIV and monotherapy for hepatitis B…chronic hepatitis B. Pegasys has reproducible efficacy, well established safety and broad to patient types with poor prognostic factors. HCV genotype 1, [inaudible], cirrhotics, heavy weight, African American, Latino ethnicity greater than 99% of patients who achieved an SVR with Pegasys remain virus negative long-term. Due to its pharmacokinetics Pegasys's packages are ready to use pre-filled syringe doesn't need to be dosed by weight, has one standard dose of 180 mcg subcutaneous per week for all patients except an [inaudible] stage renal disease.

Since the last P&T committee meeting and post June of your scan here there are two non-industry sponsored trials [inaudible] comparing Pegasys to [inaudible]. They are published in peer view journals as E pubs prior to paper publication. Both studies showed significantly greater SVR for Pegasys compared with pegintron in patients with genotype 1 for 48 weeks. Genotype 1 relapse rates for 48 weeks of full dose combination therapy of consistently range from 19 to 25% pivotal and independent

trials. The 32% relapse rate recently published in Ideal falls outside these data and then the recent paper New England Journal of Medicine authors of Ideal recognize the study does not offer a direct comparison of the pegylated interferons, only of regimens due to differences in initial ribavirin dosing and in the procedure for ribavirin dose reduction.

Safety is detailed in the Pegasys [inaudible] package inserts as you've noted, which were updated July 2009 and all of these references are available upon request. Thank you for your time and consideration.

Vyn Reese: Thank you. Questions from the committee? No questions? Thanks.

Vandana Slatter: Thank you.

Vyn Reese: Isaac Lloyd, Merck.

Isaac Lloyd: Good morning. My name is Isaac Lloyd. I'm the Medical Science Liaison with Merck Pharmaceuticals. I'd like to thank the committee for taking the time to consider pegintron on the Washington State Medicaid formulary. Currently pegintron is the preferred pegylated interferon on the Washington State Medicaid formulary. First of all I'd like to point out two unique indications for pegintron. Pegintron is the first and only approved pegylated interferon in combination with ribavirin for pediatrics indicated for children ages 3 and older with chronic hepatitis C. Also just recently pegintron became the only pegylated interferon to receive the indication for re-treatment. Of previous interferon and pegylated interferon plus ribavirin treatment failures, relapse and non-responders based on the data from Epic 3.

I would also like to point out the results of the Ideal trial, which was recently published in the New England Journal of Medicine. It compares the two pegylated interferon regimens. Top line results of the Ideal trial, a perspective study of over 3,000 genotype 1 patients here in the United States. Overall SVR rates were observed in the three treatment regimens for pegintron 1.5. It was 40%. Pegintron 1.0 was 38% and in Pegasys it was 41%. However, there were a lower percentage of patients of the pegintron groups that relapsed after end of treatment. 24% for the 1.5, 20% for the 1.0 and 32% for the Pegasys respectively. A separate analysis of 52% of patients who were assigned equal amounts of ribavirin regardless of treatment regimen supported similar SVR rates 1.5 40%, 1.0

38% and Pegasys 38%. There was however a difference in relapse rate again. Lower for pegintron at 22% for the 1.5 and 20% for the 1.0 and 35% for the Pegasys regimens. There were two changes to the PI based on the Ideal trial. First of all, ribavirin dose was increased for patients that are over 80 kg on the…previously they were on 1000 mg and now they are indicated for 1200 mg due to decreased efficacy. Second, if you need a dose reduction pegintron is now recommended at two-stage dose reduction from a 1.5 dose reduced to 1.0 and then .5.

Another unique indication for pegintron is weight based dosing. Patients weighing more than 165 pounds of 75 kilograms have lower SVR rates when flat but dosed interferon based therapy is administered. Pegintron is the only pegylated interferon that offers individualized weight based dosing and in published studies weight based pegintron demonstrates similar response rates regardless of weight. So in summary, because of these unique properties I ask the committee to please keep pegintron on formulary. Thank you.

Vyn Reese: Thank you. Any questions from the committee? Thanks. Okay. Now I'll open it for discussion. I'll also take a motion just to reiterate our prior motion.

Jason Iltz: This is Jason. I just have a question really from a standpoint of how we ensure these medications are being used appropriately and safely. Do we require any sort of feedback from the prescriber or anything that after a certain amount of time that, you know, viral loads are decreasing or have gotten to points where they need to be or there's LFTs being monitored or blood dyscrasias being looked at. Is that being done at all with this class of medications?

Jeff Thompson: So this is Jeff Thompson. Currently we are not doing that albeit I do know that several Medicaid states are actually looking at, you know, viral loads and looking at weeks of use and if the viral titer does not come down it's an indication of failed therapy and not to continue therapy. And so what, I think after the New Year it's something that we might want to work with Alabama Medicaid, which has really started I think this along with Missouri and Arkansas Medicaid. It's difficult because in the claims-based system viral titers don't necessarily mean anything to a pharmacy. So it would be something we'd have to work with the clinical community.

But it has been shown to, I think improve quality and safety in those Medicaids.

Jason Iltz: Thank you.

Vyn Reese: Any other questions or comments? I'll take a motion to reiterate the prior motion.

Jason Iltz: This is Jason. I move that we reiterate the previous motion from December 17, 2008 for the hepatitis C PDL medication class.

Vyn Reese: Second to that motion?

Ken Wiscomb: This is Ken Wiscomb. I'll second.

Vyn Reese: Okay. All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The motion has passed. The next scan is on nasal corticosteroids. Is Kim Peterson on the line?

Kim Peterson: Yes, I'm here.

Vyn Reese: Okay. Just a sec. We're just trying to get the slides up.

Kim Peterson: Okay.

Vyn Reese: That's the wrong order. We need…it's not opioids. That's not the right…we're looking at nasal corticosteroids.

Kim Peterson: You ready?

Vyn Reese: No. There's been a little bit of difficulty with the...here we go. We've got it now. Thanks. Go ahead.

Kim Peterson: Okay. So these are the findings from the August 2009 scan of our review on nasal corticosteroids and it's the first scan for consideration of the second update of this review. Next slide.

So the last full update was update number one and it was completed in June of 2008. Next slide.

So over the next few slides we have the inclusion criteria. For populations we included both adults and children with seasonal or perennial allergic or non-allergic rhinitis. And for interventions there's eight drugs as listed and the newest ones are ciclesonide and fluticasone furoate, which I believe were added in the last update at which time there were not yet any published head-to-head trials available for either of those agents. Next slide.

For effectiveness efficacy outcomes we have symptomatic relief and onset of action and then we have the usual harms outcomes, overall adverse events, withdrawals due to adverse events, serious adverse events and specific adverse events. Next slide.

So here's the details of the Medline search that we used for this scan. We started the search from the cutoff date of the last update, which was September 2007 and then we searched through July of 2009. And we found a total of 44 new citations. So we applied the inclusion and exclusion criteria that I just outlined. Next slide.

That led to narrowing it down to identifying 14 new relevant trials that met all of the criteria. And among those only one was a head-to-head trial of one of the newer drugs, fluticasone furoate for which we previously haven't had any head-to-head trials and in this trial fluticasone furoate was compared to fluticasone propionate in people aged 16 or above for treatment of Japanese cedar pollinosis. Otherwise the remainder of the trials were placebo-controlled. The majority of which involved fluticasone furoate. Next slide.

And we also searched the FDA and Health Canada websites for information on new drugs, new indications and new safety alerts and this slide reflects the main findings from those searches. So we didn't find any information about any new drugs and for new indications we found that in September of 2008 triamcinolone received approval for treatment of seasonal and perennial allergic rhinitis; specifically in really young pediatric patients between the ages of 2 to 5 years. And for new safety alerts we did not find any new black box warnings or any other serious safety alerts. So really very little in this scan. Just the one head-to-head

trial and then some placebo-controlled trials and a new indication for triamcinolone. So that's the last slide and so that concludes the summary of the new evidence and based on the new evidence the DERP participating organizations voted against pursuing a full update of this review. So the next time that this topic will be considered for update will be approximately August of 2010. So that leaves the last…final report for update number one as the most recent report. So I'll turn it back over to you now to discuss the new evidence and ask questions.

Vyn Reese: Thank you, Kim. Any questions from the committee? I'll take a motion to approve this scan.

Carol Cordy: This is Carol Cordy. I move to approve the scan.

Vyn Reese: A second?

Alvin Goo: This is Alvin. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Scan's accepted. There are two stakeholders who would like to speak and the nasal corticosteroids. The first is Dr. Meredith Zarling from GSK.

Meredith Zarling: Good morning and thank you for the opportunity to speak to you about veramyst. My name's Meredith Zarling and I'm a Regional Medical Scientist with GlaxoSmithKline. I'd like to present to you information in support of using veramyst first rather than generic fluticasone propionate. Veramyst is indicated for the treatment of symptoms about seasonal and perennial allergic rhinitis in patients starting as young as two years of age; one of only a few products with this indication.

Veramyst is a high binding affinity to the human glucocorticoid receptor with 1.7 times more binding affinity than fluticasone propionate. Second, veramyst is the only nasal steroid proven to help relieve not only all four nasal symptoms including congestion, rhinorrhea, itching and sneezing, but it is also unique from other nasal steroids in regard that it was proven in five prospectively designed studies to help relieve ocular symptoms of

seasonal allergic rhinitis such as itching and burning, tearing and watering and redness in patients 12 years of age and older. No other nasal steroid has prospective replicated studies showing consistent ocular effects and that includes fluticasone propionate.

Third, the unique device is an important attribute of this product. The device is innovative and designed based on feedback from both patients and physicians. It has a side actuator which releases a consistent dose of low volume mist, which is half that of fluticasone propionate. And I'm going to demonstrate. So this is a completely unique device. It also has a shorter nozzle and that is assists in ease of administration especially in pediatric patients.

Adverse events with veramyst in clinical trials were similar to those reported with other nasal steroids and placebo. Common adverse events reported in clinical studies were headache and epistaxis.

To summarize, veramyst is approved for patients as young as two years of age for both seasonal and perennial allergic rhinitis. It's the only nasal steroid available with proven ocular symptom improvement and is available in this unique nasal delivery system. Based on these advantages over fluticasone propionate I'd like to ask the committee to add veramyst as the preferred nasal corticosteroid available for Medicaid patients in the State of Washington. Thank you.

Vyn Reese: Thank you. Are there questions from the committee? Okay. Thanks.

Meredith Zarling: Thanks.

Vyn Reese: The next speaker is Dr. Dan Manning from Merck.

Dan Manning: Good morning. My name is Dan Manning and I am a PharmD with Merck Medical Affairs and I'm here to talk about Nasonex or mometasone furoate. I really want to talk a little bit about the difference between mometasone furoate and the generic fluticasone. One of the things with Nasonex is it has a broad range of indications for your patient. It is [inaudible] based, it's scent free and alcohol free and it's indicated down to two years of age, which is one of the lower ones in this class. It's also the only nasal steroid indicated for the prophylaxis of seasonal allergic rhinitis and it's the only nasal steroid approved for the treatment of nasal

polyps. In clinical studies it's shown to have a total systemic bioavailability of less than 0.1% and also in clinical studies, safety studies it shows no HB access oppression in the pediatric and the adult population.

I'd just like to take this time to ask you guys to consider Nasonex on the PDL. Thanks for your time.

Vyn Reese: Thank you. Questions from the committee? Okay. That concludes the stakeholder comment. Is there any discussion? I have one question. I'm not sure why that last line was on there.

Jeff Graham: This is Jeff Graham. Apparently that showed up in our minutes, the tapes, and I'm not sure why we didn't catch that because it has nothing to do with the motion.

Vyn Reese: It sounds like that should be deleted unless there's some reason to keep it. I mean it sounds like a mistake.

Jeff Graham: I agree.

Vyn Reese: Yeah. So I would strike that from the motion. After that is stricken is there anybody who wants to reiterate the prior motion from the October 15th meeting?

Ken Wiscomb: This is Ken Wiscomb. I move we reiterate the prior motion from October 15, 2008.

Vyn Reese: Is there a second?

Alvin Goo: This is Alvin. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay. That's approved. Okay. The next item on the agenda is the multiple sclerosis scan and the multiple sclerosis drugs by Susan Carson.

Jeff Graham: Is Susan on the line yet? She should be momentarily.

Vyn Reese: We're a couple of minutes ahead of schedule I think.

Vyn Reese: Yeah.

Kim Peterson: This is Kim and I'm going to sign off. But I'll let Susan know that you're ready for her.

Vyn Reese: Thank you, Kim.

Jeff Graham: Thanks Kim.

Kim Peterson: Okay. Bye.

Vyn Reese: Are you on?

Susan Carson: Hello?

Vyn Reese: Is this Susan Carson?

Susan Carson: Yes, it's Susan. Hi.

Vyn Reese: Hi. It's Dr. Reese.

Susan Carson: Hi.

Vyn Reese: We've got the first slide up and if you're ready we're ready.

Susan Carson: Okay. I just want to make sure this is the MS drugs scan first?

Vyn Reese: That's correct.

Susan Carson: Okay. All right. So I'll just go ahead on the first slide. This is the second scan for update number one of our report.

The next slide shows the history. The original final report was completed in July of 2007 and then we did a previous preliminary update scan last June, June 2008.

Slide 3 shows the inclusion criteria for our report. We included adults with multiple sclerosis and the four different kinds are shown on the slide. We also included adults with clinically isolated syndrome also known as "first demyelinating event", first clinical attack suggestive of multiple sclerosis or monosymptomatic presentation. Those are all other terms for clinically isolated syndrome. Next slide.

Slide 2 [on slide 4] shows the five drugs that we included glatiramer, interferon beta-1a, interferon beta-1b, mitoxantrone and natalizumab.

Next slide shows our inclusion criteria. The effectiveness and efficacy outcomes are shown. We looked at harms and we also looked at the occurrence of interferon beta neutralizing antibodies, their persistence and their impact on clinical outcomes.

Moving on to slide 6 for this scan we looked at the literature through July 28th, 2009 and our search identified 103 citations, which we then reviewed. Next slide.

Slide 7. Of the 103 citations we identified 8 potentially relevant trials. These included 2 head-to-head trials; 1 of interferon beta-1a versus glatiramer and another head-to-head trial of intermuscular interferon beta-1a versus subcutaneous interferon beta-1b. So it's Avonex versus Rebif. And then we also identified two secondary analyses of trials that were already included; the AFFIRM trial and the BENEFIT trial and four other various active trials or dose ranging or combination treatment trials. And then in the previous scan there were three new trials head-to-head and four secondary publications of already included trials and this included secondary analyses from AFFIRM, BENEFIT, Sentinel and the full results from the evidence trial, which is a head-to-head trial.

Moving on to slide 8 the FDA and Health Canada we searched for new indications, new drugs and new safety alerts. No new drugs. There was a new indication for glatiramer for reduction of relapses in patients with relapsing-remitting multiple sclerosis, including those who have experienced a first clinical episode and have MRI features consistent with MS. There was a new safety alert related to natalizumab. Two cases in Europe of PML were identified in patients who were on monotherapy. This is a known risk but these were the first cases that were not seen in combination therapies. These are the first cases in monotherapy. So this

is a risk that is already monitored for in patients who are on this drug, but the new addition is seeing it in monotherapy.

So that concludes the evidence we found for the scan. Just to update you the participating organizations of DERP did vote to update the MS drugs and report. We're working on that now. That is due April 2010 and the final report will be completed in June 2010. Thank you. Any questions?

Vyn Reese: Yeah. This is Dr. Reese. I have one question, Susan. As I remember PML is 100% fatal. Is that right?

Susan Carson: Yeah, that's what the FDA warning says that it's usually fatal.

Vyn Reese: Okay. All right. Thanks. Any other questions from the committee? I'll take a motion to accept the scan.

Barak Gaster: This is Barak Gaster. I move to accept the scan.

Vyn Reese: I'll take a second.

Carol Cordy: This is Carol Cordy. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Scan's approved. Okay. We have several stakeholders who would like to speak. I want to remind them you have three minutes each. So please don't go over that. The first person on the list is Debra Maas and on deck is Holly Hawker.

Debra Maas: Thank you for the opportunity to speak about the multiple sclerosis disease modifying therapies as they relate to the Washington State Medicaid formulary. My name is Debra Maas and I am the Community Outreach and Advocacy Coordinator for the National MS Society in Washington State.

In a region where MS is more prevalent than almost anywhere else on earth our chapter is the most dependable resource for programs, services, education, information and support to 9,000 people living with MS; to

50,000 family members and friends who care about them and to our entire community. I will leave you with an expert opinion paper on disease management written by the National Clinical Advisory Board of the National MS Society, which sites the information I'm providing you today.

The Society recognizes that the factors that enter into a decision to treat are complex and best analyzed by the individual patient's neurologist. Patient's access to medication should not be limited by the frequency of relapses, age or level of disability. Treatment is not to be stopped while insurer's evaluate for continuing coverage of treatment as this would put patients at increased risk for recurrent disease activity. Therapy is to be continued indefinitely unless there is a clear lack of benefit, the side effects are intolerable or better therapy becomes available.

All of the FDA approved agents should be included in formularies and covered by third party payers so that physicians and patients can determine the most appropriate agent on an individual basis. Failure to do so is unethical and discriminatory. Movement from one disease modifying medication to another should occur only for medically appropriate reasons. The management of MS has been substantially advanced by the availability of all six of the FDA approved disease modifying agents. The benefits of these agents include direct evidence of disease modification. Significant obstacles to obtaining these agents exist for appropriate candidates with MS. One is misunderstanding by some policy makers and insurers of the benefits of disease management therapy leading to inadequate coverage both initially and long term.

Approximately 400,000 Americans have MS and every week about 200 people are diagnosed. Worldwide MS affects about 2.5 million people because the Centers for Disease Control and Prevention does not require U.S. physicians to report new cases and because symptoms can be completely invisible the numbers can only be estimated. With a passion for bringing about a world free of MS the National MS Society helps everyone affected by the disease to live…

Jeff Graham: Please conclude your remarks.

Debra Maas: ...to live richer, healthier and more independent lives.

Vyn Reese: Thank you. Any questions from the committee? Thank you. The next person is Holly Hawker. On deck is Dr. Eugene May.

Holly Hawker: My name is Holly and in 1998 at the age of 20 I was diagnosed with multiple sclerosis. At that time there was no treatment for MS. We could treat some symptoms, but could do very little for the disease. At the time I was attending college and working full-time in my chosen career. For about five years I was periodically disabled and unable to work and maintain my college attendance. For someone in her mid 20s life looked pretty hopeless and frightening.

In the early 90s disease altering interferons came to market and I started on betaseron a subcutaneous injection. My symptoms improved and my attacks became less frequent. However, I experienced severe site reactions and side effects to the point that I considered discontinuing my medication. In 1998 because of my frustrations my neurologist suggested another interferon, Avonex, which is an intramuscular injection. Within a few months on Avonex my symptoms were greatly improved, site reactions were non-existent and the side effects were minimal. I became more active than I was before my diagnosis and I'm virtually symptom free. I work full-time, have a seven-year-old daughter, exercise at least five days a week and have a variety of active hobbies. On Avonex I have had one significant attack in over 10 years.

Avonex has allowed me to conquer one of my greatest fears with this disease. It has helped me remain a contributing member of society. Because MS is a different disease for everyone, every person with MS may react differently to the limited medications available. Throughout my work and experience with the MS community I have spoken with many people about their medications and experiences. Many people with MS cannot tolerate the interferons and have success with Copaxone or Tysabri. Others can only tolerate the interferons or like myself only specific interferons. Without access to the options that are currently available and new options that we hope will be introduced soon we are not allowed to find the treatment that works for us and create our own success story.

I have come here to ask that you consider the remarks of Dr. May, myself and others and allow coverage for all disease modifying MS drugs. The

entire collection of the limited medications available provides a potential life changing tool for all of us with MS.

Vyn Reese: Thank you.

Holly Hawker: Thank you.

Vyn Reese: Questions from the committee? Thanks. Next speaker is Dr. Eugene May. On deck is Dr. Lynda Finch.

Eugene May: Thanks for letting me come and talk today. I'm a Neurologist in Seattle. I work at the MS Center at Swedish. I'm in private practice and a member of that group, but I'm also here as a member of the board of directors of the Washington State Neurologic Society and also as a member of what's called the Puget Sound MS Alliance, which is a group of neurologists who specialize in MS care and meet on a regular basis to discuss clinical care and research issues. The point of my being here is to urge you to continue to make available to all MS patients who use DSHS for their medical care to have access to all of the MS medications in the future allowing the neurologists to make the choice of which MS medication to use in their cases based entirely on medical basis and not formulary availability. I know based on the data that's already been presented that you have access to the data from large pivotal studies and comparative studies that in a gross general sense show that the MS medications are for the most part relatively equally efficacious. But a number of studies that are smaller than the pivotal studies in the comparative studies show pretty definitively that the MS medications have some relative differences in efficacies when you look at other parameters such as early versus late, relapse rate, progression of disability, cognitive decline and MRI parameters. And neurologists use those variable efficacies parameters in deciding which MS medication to use in any individual MS patient at the onset of their illness and over the course of their illness. The other factor that neurologists use in deciding which MS medication to put any individual patient on is the patient's potential tolerance of side effects and that's very important because each of the MS medications has a totally different side effect profile and any individual's potential tolerance of the side effect profile is going to vary. So if there are formulary restrictions on the medications, our ability to choose side effect tolerance per patient is going to be limited.

MS is totally unpredictable. How a patient is going to respond to a medication is unpredictable. Neurologists need to have the ability to choose what medication to use in any individual patient's case at the onset of their illness and later on in their illness for medical reasons only.

I have a couple of physician statements. One is from the Puget Sound MS Alliance and one is from the Washington State Neurologic Society.

Jeff Graham: Please conclude your remarks.

Eugene May: Each of the consensus statements states definitively that the neurologists in Washington state who take care of MS patients feel that we need open access to all the medications. I don't know if there is a mechanism for me to get you guys those consensus statements, but if there is I can get those out today.

And the other issue is I can answer the question about PML being a fatal illness. It is not if the cause of the immune suppression is removed. So in the example of natalizumab in patients with MS who are treated with natalizumab, when the natalizumab was stopped and in a couple of cases where treatment was provided, where plasma exchange was provided, the patients did not die. They were left with some neurologic disability but it was not fatal.

Vyn Reese: Thank you.

Eugene May: Uh huh.

Vyn Reese: Any questions from the committee? Okay. Next speaker is Dr. Lynda Finch. On deck is Dr. Fred Amberger.

Lynda Finch: Hi. I'm Lynda Finch. I'm a Medical Science Liaison with Biogen Idec and I'm here to talk to you today about Avonex, but I also represent Tysabri and can answer any questions you might have about that drug. And Dr. May has already addressed the question about PML and I just want to confirm that it's a different…it appears to be a different disease in patients with MS than in the HIV/AIDS setting or in the transplant setting where it was seen predominantly before. So the majority of patients who have had PML are alive with varying levels of disability and that's

because we can remove the drug and those patients have a functional immune system and can reconstitute immunity in the CNS.

So back to Avonex. The a…as you know the prevention of…or postponement of disability is the most important therapeutic goal in the treatment of MS and Avonex is the only disease modifying therapy that had the prevention of disability progression as its primary endpoint in its clinical trial, phase 3 clinical trial. And it's the only disease modifying therapy with a 37% reduction…relative reduction in disability progression sustained over six months, which is the most stringent end point of disability.

I also want to remind you that Avonex is the only disease modifying therapy that has FDA approved indication for the three key areas of slowing disability progression, reducing relapses and for use after a first attack. And I want to share some new very compelling data about long-term treatment of MS with Avonex. So at a…at a [inaudible] this year we presented our results from our perspective open label follow up study, which is a 10-year study of patients who presented with a first event. And what we've shown is that early treatment continues to show an effect on reducing the risk of disease conversion out 10 years later. So the patients who were treated immediately with Avonex had a statistically significant 40% reduction even 10 years later to the progression of CDMS, which is clinically definite MS. And furthermore, and even more importantly, these patients remained fully functional. So we had 80% of the patients in this study at 10 years were still below an EDSS of 3.0, which is critical because patients are still fully functional at that level of EDSS.

If you didn't treat these patients what you would expect is only 25% of them would be at that level of functionality. And then at [inaudible] last year we reported our long-term results from our assurance study which was the extension of our phase 3 pivotal trial with MS patients. This is, again, showing results that we lower EDSS scores from baseline and had significantly lower progression to key EDSS milestones. We also saw improvements in quality of life and patients maintain a greater sense of self-sufficiency and independence compared to those that weren't on Avonex.

Jeff Graham: Please conclude your remarks.

Lynda Finch: So just to conclude that Avonex has important benefits for patients. The key items are the efficacy it provides in slowing disability progression, convenience of a once weekly injection, which results in improved compliance and fewer injection site reactions. And then if you have any questions about Avonex or Tysabri I would be happy to address them.

Vyn Reese: Thank you. Questions from the committee? Okay. Thank you. Next speaker is Dr. Fred Amberger and on deck is Dr. Robert Martin.

Fred Amberger: Good morning. I'm Fred Amberger. I'm a Scientific Director with Novartis and I'm speaking this morning on behalf of Extavia. Extavia is approved by the FDA for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations. The therapy is also indicated for patients who have experienced a first clinical episode of MS and have features consistent with the disease as shown by an MRI. The same medicinal product is betaseron. Extavia offers patients and physicians a new branded version of interferon beta-1b, a first line disease modifying therapy that has been a standard of care for MS for the last 16 years.

Patients with a prescription for betaseron or Extavia may be able to use either product without compromising safety or efficacy. Novartis gained the rights to seek approval for its own branded version of interferon beta-1b through agreements with Bayer Schering, the company that markets betaseron. Betaseron is a registered trademark of Bayer Schering Pharma AG. Interferon beta-1b has been shown to reduce annualized relapse rates by 34% with patients nearly twice as likely to remain relapse free for more than two years compared to those receiving placebo. In addition, treatment with interferon beta-1b may slow disease progression. After two years almost three-quarters of patients who experienced a single episode of neurological disease lasting 24 hours or more did not progress to clinically definite MS.

In the interest of time I'm going to resist the temptation to list the lengthy adverse events as they've been, I think, well documented. If there are questions, please see the prescribing information.

MS is unpredictable and can be difficult to manage. Support programs are an essential element to help patients and physicians effectively management this difficult disease. Along with the prescription for Extavia, patients will be given an option to access a patient support

program. This program includes a number of services. Nursing support services are provided which include one-to-one injection training, patient education and toll free product support. Patient training includes an injection training kit, instruction sheet, carrying case and injection training booklet. Additional topics may include managing injection site reactions, lifestyle management topics, diet and exercise and stress management.

To summarize, Extavia is interferon beta-1b. The clinical studies that were given to the FDA were the same ones that were given for betaseron. OHSU did not include Extavia as a branded product in their review, but they did review interferon beta-1b. Thank you.

Vyn Reese: Thank you. Questions from the committee? Next up is Dr. Robert Martin. On deck is Walt Corneille.

Robert Martin: Good morning and thank you for the opportunity to speak to the group. My name is Robert Martin and I'm a Medical Scientific Liaison for Bayer Healthcare Pharmaceuticals, makers of betaseron. I will limit my comments to just new data that's been published within the last year.

Our ongoing clinical trial in early MS benefit is a five-year prospectively planned randomized multi-center, placebo-controlled trial of 468 patients. As part of the prospective design of this trial data was published at years two, three and five. The five-year data was just published in September of this year in the Journal Lancet. There's lots of great information in there, but I'll focus on just one item, one outcome, and that is with cognitive function. In the BENEFIT trial cognitive function was measured using the PACAT test. That stands for the Paced Auditorial Serial Edition Test. That's a validated reproducible cognitive function test and at five years in this BENEFIT trial, patients who received early treatment with betaseron had significantly better cognitive functions as assessed by the PACAT scores compared with patients who had delayed treatment.

Again, changes in cognitive functions are important. They affect a patient's quality of life and they can be a reason for departure from the workforce. So in conclusion, remember that there are a lot of interferon choices out there and that, you know, patients have different needs and again I would encourage the committee to maintain the open access that they have in the past including interferon beta-1b betaseron. Thank you.

Vyn Reese: Thank you. Questions from the committee? Next up is Mr. Walt Corneille.

Walt Corneille: My name is Walt Corneille. I was diagnosed with relapsing remitting multiple sclerosis in 1996, a disease I recognize has been affecting my body since back in the 1976 area. The problem…if I'd been diagnosed in '76 there was nothing anybody could have done for me. I have been on two disease modifying drugs—Avonex and now Tysabri. I have stayed fairly stable. I don't have a lot of relapses. When I do have relapse it's not that severe. I have to attribute that to the medications I have been involved with courtesy of my neurologist. I ran into my neurologist the other day. I hadn't seen him in several years because I transferred care up to the University of Washington Medical Center and he said, "Gosh, you look great." He had diagnosed me back in '96 and I said, "Well, do I really?" He said, "No. You look good. I hadn't expected somebody to be moving around as well as you move around over all these years of having been diagnosed." So I appreciate the availability. I've been on two different disease modifying drugs. I tolerated the side effects fairly well, but I've also been able to stay very active. I do a lot of volunteer work with the National MS Society and just in my general society as far as my involvement and volunteer work I do generally. So we appreciate your making these disease modifying treatments available and make them readily available. I'll be happy to answer any questions.

Vyn Reese: Thank you. Any questions from the committee? Okay. I'll open the topic for discussion. If there's no discussion we can turn our attention to the previous motion. We basically had open access before. I don't see any new evidence. One thing we might want to strike though is safe. They're efficacious and they're worth the risk, but they're not always safe.

Jason Iltz: This is Jason. I would move that we reiterate the motion as stated on August 20th, 2008 for the class…PDL class of multiple sclerosis drugs.

Vyn Reese: Is there a second?

Ken Wiscomb: This is Ken Wiscomb. I'll second it.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. It's approved. Next item on the agenda is the scan review of the TZDs. Is the presenter on line?

Susan Carson: Yes. This is Susan. Do you have the slides up?

Vyn Reese: Right. The TZD slide is up.

Susan Carson: Okay. Thank you. Okay. Yes, this is the first scan for update number 2 of the DERP thiazolidinediones report or TZDs.

If you go to slide 2 it shows the history. The last report was completed in August 2008. That was update number 1. That report had searches through November 2007.

Slide 3 shows our included populations. We looked at adults and children with type 2 diabetes, with prediabetes or metabolic syndrome. Next slide.

We're on slide 4. There are two TZDs, pioglitazone and rosiglitazone, Actos and Avandia are the brand names. So in our report we looked at both a head-to-head comparison of the two TZDs or studies of a TZD versus placebo or no treatment.

Next slide shows the outcomes. Intermediate outcomes were glycemic control or A1C and we also looked at effectiveness outcomes. For type 2 diabetes we looked at microvascular and macrovascular disease. All cause mortality and quality of life as well as durability of control. For prediabetes we looked at the incidence of the development of type 2 diabetes. Next slide.

We looked at the usual harms in our report.

Moving on to slide 7. For this scan we searched Medline from November 2007 to August 2009 and we found 243 citations. Next slide.

Slide 8. After review of those 243 citations we identified 22 potentially relevant new trials. Fifteen of those were either placebo or active control efficacy trials. Two were head-to-head efficacy trials.

So then the next slide, slide 9, continues the description of the trials we identified. There were two new effectiveness trials. The first was the RECORD study, which looked at rosiglitazone plus metformin or a sulfonylurea versus metformin plus a sulfonylurea. The interim results of the RECORD trial were previously published and they're in the current report. But this is the updated result. And then we also identified another effectiveness trial which looked at cardiovascular mortality and hospitalization for heart failure in…for pioglitazone versus Glyburide in patients who have heart failure. And then finally there were three post hoc analyses of trials already included, the PROActive trial and the ADOPT trial. There were two publications from PROActive. In patients with chronic kidney disease and those with peripheral artery disease. And then the publication from the ADOPT trial looked at fracture rates.

Our next slide, slide 10, is the last slide. We identified no new drugs or indications. So just to update you the TZDs report will not be incorporated into the larger diabetes drugs report, which is in process now. We're drafting the key questions. So this information will be updated. It just won't be its own separate report anymore. I'll take any questions if you have them.

Vyn Reese: Any questions from the committee? I'll take a motion to approve the scan.

Ken Wiscomb: This is Ken Wiscomb. I move we approve the scan to this adequate update.

Vyn Reese: Is there a second?

Carol Cordy: This is Carol Cordy. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The scan is accepted. We have four stakeholders who would like to speak. The first is Dr. Rob Pearson and on deck is Dr. Mark Nathan.

Rob Pearson: Hi. Good morning. My name is Rob Pearson. I'm a Pharmacist with the Research and Development Division of GlaxoSmithKline. So I'd like to

start by thanking the committee for this opportunity to present some new information that's become available about the safety and efficacy of Avandia over the past year.

There were two large prospective outcomes, trials that were presented this year. Both at the American Diabetes Association meetings. This included the RECORD trial, which was on the scan as well as the BARI 2D trial. These were both published subsequently in the New England Journal of Medicine, as well as in the Lancet for the RECORD trial. So the data from the RECORD trial, which included 4,400 patients who were followed for five to seven years demonstrated no increase in cardiovascular events with Avandia compared to metformin and sulfonylureas. And more importantly in this trial, this documented Avandia's ability to sustain glycemic control for over five years in this trial, which no other oral anti diabetic medication has done.

The BARI 2D trial, the second of these two big outcomes trials was sponsored by the National Institutes of Health and this included very high risk patients with long-term diabetes, over 10 years, as well as known cardiovascular disease. So again in this high risk population Avandia was not only found to be safe, but when used with metformin was able to significantly gain and sustain glycemic control compared to the insulin providing strategies in this trial.

With many medications out there and available for the treatment of our patients with diabetes it's reassuring to look at the trial and research portfolio behind Avandia with over 1.9 million patients years of clinical trial data ranging from prediabetic patients out to late stage diabetic patients. Avandia is the only TZD with a cardiac outcomes trial that met its primary endpoint and only Avandia has been proven to sustain glycemic control for up to five years in multiple randomized trials. And in addition to this, about a month ago the American Association of Clinical Endocrinologists updated their diabetes treatment algorithm which reaffirms the use of Avandia as monotherapy and in combination therapy for the treatment of type 2 diabetes and it also specifically references the durability of this class and of Avandia for the treatment of these diabetic patients.

So the bottom line is that of course here in Washington diabetes is certainly a leading cause of morbidity and mortality and the clinicians that

care for patients here, you know, need access to the full armamentarium of medications for these patients. And because of the solid efficacy profile of Avandia I would like to respectfully request that the committee maintain Avandia as a preferred product for the Medicaid patients here in Washington. Thank you very much. If you have any questions I'd be happy to address those.

Vyn Reese: Thank you. Any questions from the committee?

Rob Pearson: Thanks.

Vyn Reese: Our second speaker is Dr. Mark Nathan and on deck is Dr. Tom Aoki.

Mark Nathan: Good morning everyone. My name is Mark Nathan. I'm a Practicing Interventional and General Cardiologist. I'm here to provide testimony and support of maintaining Avandia on your formulary. I've been a speaker for GlaxoSmithKline for a number of years in their metabolic product line but for today I'm in my own capacity unpaid basically to help you understand the need to maintain access to the TZD class of drugs.

GSK did not participate in the preparation of any of these comments. So my purpose is to bring you as a committee up to date on some new information that was generated in the last year or so.

For the past 10 years it's actually been controversial as to whether glycemic control significantly improves event rates in macrovascular events, myocardial infarction and stroke. In fact, the randomized control trials have generally been inconclusive. But this summer two large meta-analyses involving some 30,000 patients and 165,000 patient years were published—one in the Lancet and one in the Journal of Metabolic Nutrition. Now both of these trials…or I should say two out of the trials involved the TZD class of drugs. One was PROActive and one was ACORD, which were referenced in your scan. It was interesting that both trials were concordant with one another and basically conclusively demonstrated that there was a 17% reduction in the incidence of non-fatal myocardial infarction and a 15% reduction in coronary heart disease events thereby putting at rest the question as to whether glycemic control is important for cardiovascular patients. Now the ADOPT trial and the RECORD trial that you heard about both in the scan and the previous speaker basically both confirm that rosiglitazone was superior to either a

sulfonylureas or metformin in durability of glycemic control over a timeframe of about five years. Since the reduction in myocardial infarction or other macrovascular or microvascular event rates depends on continuing glucose control. It's obviously important to have access to a drug which will maintain that sugar control over a period of time.

Now as the previous speaker just mentioned the new ACE guidelines highlight the particular strengths of the TZD class and elevate them to a preferred agent in patients with metabolic syndrome and non-alcoholic fatty liver disease. Avandia lowers blood sugar without much hypoglycemia. This is important because hypoglycemia has been implicated in cardiovascular adverse events in treating patients with diabetes. Avandia also improves the lipid profile in a patient, which is why it is favored in metabolic syndrome patients. And patients with statins often have elevated liver function tests. In most cases this is actually due to fatty liver rather than a toxic affect of the statins and it is possible that the use of TZDs may help these patients quite a bit.

Now the RECORD trial confirms the safety of Avandia in patients with coronary vascular disease. Specifically in the RECORD trial there was no increase in cardiovascular death or cardiovascular hospitalization in these 4,500 patients over four years. Now following a possible safety signal for ischemic heart disease in March of '07 the FDA launched an extensive investigation and concluded in November '07 that there's no difference between TZDs and other oral anti diabetic drugs in the safety and coronary patients. But definitive proof came just two months ago…

Jeff Graham: Please conclude your remarks.

Mark Nathan: …when Menuchi(?) published a meta-analyses of 164 trials and 43,000 patient years in which it showed that there was absolutely no difference whatsoever between Avandia and any other comparator including placebo or other oral anti diabetic drugs. So with the exception, in conclusion, of a signal for increased fluid retention and possible congestive heart failure in patients who are susceptible to fluid overload the use of the TZDs is both effective, beneficial and safe in patients with coronary heart disease. Thank you.

Vyn Reese: Thank you. Any questions from the committee? Okay. Thanks.

Mark Nathan: Thank you.

Vyn Reese: Next up is Tom Aoki and on deck is Dr. Arnold Pollack.

Tom Aoki: Good morning. I'm Tom Aoki. I'm a Professor at the University of California Davis Medical Center, Division of Endocrinology and Metabolism. A brief background, I attended Yale Medical School, did my residency at Yale. Became very interested in diabetes and ended up at the Joslin Diabetes Center where I remained for 15 years and [inaudible] the ranks at Harvard. Became head of the Metabolism at Joslin and left to become Division Chief and Professor at the University of California Davis.

I should mention from the outset that I have been…I am a former member of the FDA Advisory Committee on endocrinologic and metabolic drugs and currently am a consultant to that same committee.

I have been a strong proponent of the use of TZDs from the…when [inaudible] first made its appearance and continued to be a very strong supporter of the use of TZDs up to the present.

I believe that my whole philosophy in treating diabetes is that to treat diabetes one must normalize the biochemistry and physiology of the diabetic patient and that glucose control is part of that. The TZDs provide a very unique series of actions that actually do seem to move in that direction of normalizing the biochemistry. It's not surprising then to find out that not only does it improve blood glucose control, lower free fatty acid level, lower insulin…circulating insulin levels, decreasing pH1 and I think I mentioned decreased systolic and diastolic blood pressure, decreased inflammatory markers like IL6, IL8 and high sensitive c-reactive protein.

For these reasons alone…well, let me back off on that statement. Two things that are very important attributes of the TZD and Avandia in particular is that it slows down the progressive loss of pancreatic beta cell function. In the [inaudible] prospect of diabetes studies it was determined using the homeostasis model assessment equation that one from the time of diagnosis of type 2 diabetes one experiences the loss of pancreatic beta cell function at the rate of 4% per year. In the ADOPT study that you've already cited that was shown to be decreased by the use of Avandia to 2%

per year. So a person will not run out of pancreatic beta cell function following the diagnosis of diabetes in 12 years, but rather closer to 25. Hence the drive toward the maintenance of normal biochemistry and physiology is really very strongly supported by the use of the TZDs. I feel very strongly that TZDs, Avandia in particular, should be considered first line drugs ahead of sulfonylureas and certainly ahead of metformin because of the attributes of decreasing insulin resistance and slowing the loss of pancreatic beta cell function; something that we cannot at this point in time regenerate. Thank you.

Vyn Reese: Thank you. Questions? Thanks. Next speaker is Dr. Arnold Pollack.

Arnold Pollack: I'm Arnold Pollack. I'm a cardiologist in Burien and I actually do speak for Takata Pharmaceutical. But this is something very, very important to me because I treat diabetics all the time. Patients who have diabetes are going to die a cardiovascular death most of the time. They are going to die on my doorstep. Drugs that critically impact cardiovascular disease and what we call macrovascular outcomes, that's stroke, heart disease, heart attack, are diseases that are very, very critical. Pioglitazone, Actos and Avandia are classic TZDs that if you had excellent descriptions of the four they're a critical class that impact this disease.

I want to mention and add to your database…there's a couple of trials that weren't previously mentioned. PARISCOPE in particular and CHICAGO. Those are studies that have used pioglitazone that have actually showed improvement in cardiovascular plaque and carotid intimal thickness. They actually positively impact the disease. That has been critically difficult over the many years of actually showing drugs that actually positively impact cardiovascular disease. Going back as far as UKPTS showing macrovascular, cardiovascular, positive impact on impact of disease decreasing the risk of myocardial infarction, decreasing the risk of cardiovascular complications and actually showing plaque proactive in its secondary outcomes. Was it critically made? There was a study that was done in the sickest of sick cardiovascular patients and in the secondary outcome actually showed improvement in cardiac outcomes. The only problem with that trial is that they unfortunately had a vascular surgeon because there was an increase in more lower extremity revascularizations. But on the secondary endpoint, which was statistically valid there was significant improvement in cardiac outcomes, decreased MI, decreased death from cardiovascular death. That is one of the first times in all these

years that we've actually had a drug that positively impacts macrovascular outcome. I think Avandia is an excellent drug but I will mention that with all the data that's out there, and it's actually being very reassuring, the meta-analyses that was actually done by Steve Neeson(?) has put an enormous amount of fear in the patient's IC. They come into my office saying, "Avandia, wasn't that the drug that was in the news?" I think what the result is is that we're not using TZDs and I think that's not the right approach. I think you've heard all the way here that it's critically important that diabetics…

Jeff Graham: Please conclude your remarks.

Arnold Pollack: …have TZDs. So I want to encourage you to broaden the spectrum and allow a drug that has positive cardiac outcomes and be able to have TZDs more easily useful for patients who critically need it. Thank you very much.

Vyn Reese: Thank you.

Arnold Pollack: Are there any questions?

Vyn Reese: Any questions from the committee? Thanks. Any further discussion from the committee? Does anyone just want to tackle the prior motion? No volunteers?

Jason Iltz: Just a question for clarification. This is Jason. The amendment on 2008, February of 2008, what impact did that have on our previous motion from 2006?

Siri Childs: This is Siri. What we did is initially when we reviewed this drug class or when you review this drug class and we did our cost analyses, Avandia was selected as the preferred drug and then as we received information about possible risk signs we decided and it came back to the committee that both the drugs should be available and that's where it stands right now.

Vyn Reese: Right. It was the cardiac risk study on Avandia and the FDA, even though there's been other data that's come out still has a black box warning on Avandia for that one study. So it's…there are other studies that are conflicting with that study. That's why we made the decision, as I recall.

Siri Childs: Right.

Barak Gaster: This is Barak Gaster. I move that we reinstate and continue our motion dated June 21st, 2006 regarding the thiazolidinediones drug class.

Jason Iltz: This is Jason. I'll second that.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay. It's passed. The next item on the agenda is the long acting opioids and the scan is coming up. Is the presenter on line?

Susan Carson: I am. This is still Susan. So you ready for opioids?

Vyn Reese: Yeah, Susan. We have our first slide up. So we're ready to go.

Susan Carson: Okay. Thank you. Okay. So this is the first scan for what would be update number 6 for the drug class review on long-acting opioids.

Slide 2 shows the history of the report. Last report was update number 5, which was completed in April 2008 with searches through September 2007. Next slide.

Our included populations were adults with chronic non-cancer pain or acute low back pain. Next slide.

It shows…this slide shows the included drugs and we defined long-acting opioids as those which are administered three times daily or less frequently. Next slide.

Slide 5. Our effectiveness outcomes were pain control and functional status.

Slide 6 shows our harms outcomes and the study designs. For effectiveness we included controlled trials compared to any comparator.

For safety we looked at controlled trials or observational studies. Next slide.

We're on slide 7. For this scan we searched Medline from April 2007 to June 2009 and we identified 389 citations.

Slide 8. After review of those 389 we identified six potentially relevant trials and the description of those trials are shown in Table 1 in your scan document. One was a secondary analysis of a head-to-head trial of transdermal fentanyl versus sustained release morphine in patients with low back pain. Additionally, there were four active and one placebo-controlled trial and then one uncontrolled trial with just one group—one uncontrolled trial.

The next slide, slide 9, shows results of our FDA and Health Canada searches. New drugs there are generic oxycodone extended release was approved in April and generic fentanyl extended release transdermal…well, two kinds of oxycodone approved in April and July of 2008 and then a generic fentanyl extended release transdermal approved in October 2008. Next slide.

Slide 10. We identified no new indications for our included drugs. Safety alerts are listed in your scan document. They're mainly recalls due to problems in the manufacturing of the drugs leading to oversized tablets delivering too much dose. So a recall but no new black box warning.

Slide 11 just continues the safety labeling changes and safety alerts. And that concludes the presentation and I'll be happy to answer any questions.

Vyn Reese: Thank you, Susan. Question. This is Dr. Reese. Now there have been so many recalls. Are there generics available for extended release morphine and a long-acting oxycodone now or are they still being recalled and not available or what's the status?

Susan Carson: Um, you know, I'm sorry I don't have the answer to that question. I believe that the recalls were for particular lots although I, you know, I don't want to speak out of turn.

Donna Sullivan: Dr. Reese, this is Donna Sullivan. My…we had our third quarter review and I was told by our pharmacy benefit manager that oxycodone extended

release is no longer available on the market. There is no generic for OxyContin.

Vyn Reese: That was my understanding too.

Donna Sullivan: Yeah.

Susan Carson: Okay.

Vyn Reese: I wasn't sure if it had come back on yet.

Donna Sullivan: No. It came on. The generic was available. Then it was removed from the market. It came back and has been subsequently removed again.

Vyn Reese: Okay. So it happened twice. So it's still not there.

Donna Sullivan: That is correct.

Vyn Reese: Long acting morphine is okay though.

Donna Sullivan: Yes, that is correct.

Vyn Reese: Okay. All right. Thank you. Okay. Thanks, Susan. I'll take a mo…any other questions? I'll take a motion to accept the scan.

Patti Varley: Patti Varley. I'll move that we accept the scan.

Vyn Reese: Vyn Reese. I'll second. All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The scan is accepted.

Woman: There are no stakeholders.

Vyn Reese: Okay. So no stakeholders in this class. So let's look at the motion. Would anyone like to reiterate the prior motion?

Alvin Goo: This is Alvin. I move to…I reiterate the motion for long-acting opioids made on June 18th, 2008.

Vyn Reese: I'll second that motion. This is Dr. Reese. All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. It's passed. Thank you. So we're adjourned for lunch. We'll reconvene at 1:00.

Susan Carson: Thank you. Bye.

Vyn Reese: Thank you very much.

I'd like to now reconvene the committee as the DUR committee. This is Dr. Reece and our first item of business is looking at our DUR minutes. Are there any additions or corrections to the minutes? I have one. It's my comments on page 43. It's the fourth paragraph up from the bottom. It's the next to last line. A lot of words are sort of jumbled together and this is what I meant to have said. I probably garbled my speech and I think that…this should be a guideline to providers that they should start with generic drugs that are short- or intermediate-acting until they figure out the dose the patient needs. There's lots of words merged in that particular sentence. So it should read, "They should start with generic drugs that are short- or intermediate-acting until they figure out the dose the patient needs." Any other additions or corrections?

Vyn Reese: If there are no other additions or corrections, I'll take an amendment…or take a motion to accept the minutes as amended.

Jason Iltz: This is Jason. So moved.

Vyn Reese: I'll second that. This is Dr. Reese. All those in favor, say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The minutes are approved. So now, I'd like to turn the meeting over to Jeff Thompson who's going to present more data on Senate Bill 5892.

Jeff Thompson: So I passed copies of the report that have gone out [inaudible]. As soon as the handouts come around I'll [inaudible] to the audience.

Siri Childs: Jeff, use the microphone.

Jeff Thompson: So just to bring everybody back to where we were with the legislation…this is Jeff Thompson from Washington State Medicaid. 5892 had five components. Section A of that allows the agency to provide feedback reports to physicians, based on brand, generic, and DAW prescribing, and so what I've given you is copies of the actual feedback reports and an example of one of the feedback reports to an organization as well as the Generic News which we…which we put out trying to actually give some information about your decisions on preferred, nonpreferred, as well as where are the average daily costs in comparisons. And they'll be another one coming out with this next generation. So what I want to do just real quickly is just…next slide here…is 5892 basically asks the agencies to try and improve its overall generic utilization, recognizing that 80% of the spend is on 20% of the…of the utilization which is brands and vice versa when it looks at generics. Eighty percent of the utilization is generics…yes?

Male: Excuse me for interrupting. Were there handouts available?

Jeff Thompson: It's coming around. I hope there's some extra PowerPoint, but I'll make sure it's posted, if not.

Male: Okay. And Duane will post that?

Jeff Thompson: Yes. Yes. So we'll…we'll post, and I apologize. It's just been a little bit over the top lately. Our current generic utilization is around 63%. That's looking at all generic options as opposed to brand options. Many of the private plans are at 80 or better percent. The difference between fee-for-service Medicaid and some of the plans obviously are formularies and co-pays. But that said, should we not be able to get closer to where the commercials are? One would also have to say on the other side is, does Medicaid have sicker clients, and therefore, we are not able to achieve a generic, because clients are sicker. For one of those reasons is why we actually chose a generic feedback report in only six classes where there are a lot of generic options, and then that issue around mine or sicker somewhat is…becomes less.

When you start looking at the generic fill rates, we find that out of the 15,000 providers, the 7,000 endorsers, there's roughly about 1,500 providers that have a generic fill under 80%. So that really I think is good news is because many of our prescribers are out there doing a great job of prescribing generics where appropriate and brand where appropriate, but there are about 1,500 providers that have generic fill rates that are less than 80%. And now that we're getting into feedback reports that begs the question is, how do I compare myself to a peer, you know? Am I special in a certain drug class? Am I the guy that gets everybody that's allergic to the blue pill, and therefore have to give the red pill to everybody? That type of thing. And so now this statute allows us to gives feedback reports, and I think, you know, as an ex-lab tech that had to run standards controls on everything I did, I think that's what we need to do when you are a prescriber, because there's no way that you can remember the last 50 or the last 30 prescriptions you wrote to actually, you know, in your head figure out what your posi and distribution is and what your statistical analysis is with your peer, because you have no clue what your peers are doing. All you know is what you're doing. So we are actually running Z statistics based on peers, and so a peer is either a mental health professional, a primary care professional, a nurse practitioner, or is an "other" or is a pediatrician. There are five classes that we are…five peer groups.

We are running these feedback reports with only six drugs where there is a lot of generic opportunities, and it's the six drugs that were in the Generic News. It's the second generation antidepressants, the ADHD drug, long-acting narcotics, the NSAIDs, the PPIs, and the statins, so where there's generic options, and within that, we're also looking not only at brand and generic, but we're also looking at DAWs utilization.

So here's what the numbers say. So what we decided was to look to at three domains. Those who have prescribing a DAW greater than 25% or that had generic utilization that was under 80% or that was statistically aberrant from their peer...those five peer groups that I talked about, and that they had more than, I believe it was a couple hundred prescriptions, because we had to make it statistic…maybe it was actually more than 30 prescriptions. I don't remember that, but it had to be something that we could actually do some statistical analysis. And it turns out that there are 824 prescribers within our 15,000 prescribers are 7…roughly 7,000 endorsers that fit these statistics. That cohort represents, out of our $400

million about $6.6 million and 36,000 clients. I think the good news is there were only…out of the 824, there were only 6 providers that had 100% brand utilization out of all their scripts, and nobody had 100% DAW utilization. Stop me at any time.

When you look at generic use, you know, basically which is driving the cost curve? Is it DAW? Is it generic utilization, or is the difference from peer? You know, most of it obviously is in generic use, 65% on cost, 70% on clients. That's where the biggest…the biggest sort of belly of the curve is. When you look at the prescribers, it's primarily in primary care. It's not…it's not mental…all mental health there's mixed in there where other with specialties, but these are just how the numbers come up. It looks like within these six classes, albeit it's a complex analysis, that where most of the brand usage in that 6.6 million is largely in the antidepressants and ADHD drugs, but you can understand how complex it gets when you try and lump and split by those multiple domains. And then the top 50 prescribers within that 824, represent 22% of the overall cost of which will then start using some academic detailing to go out with these report cards early next year when we get the second round. Yes?

Vyn Reese: Jeff, this is Vyn Reese. I think one of the things we have to…as we're doing this…this is a great exercise…is we need to make sure that as drugs go generic, we stop restricting them. That's like Gabapentin in the chronic pain medication class. It's easier to prescribe Cymbalta or Lyrica than it is Gabapentin, because it is…it still has a lot of restrictions on it that were set when it was a very expensive brand-name drug, and now it's gone generic, and all those restrictions are still there and it's…and the other drugs…I mean, now the providers are going to write for brand-name, because they can't get the generic that easily, so…

Jeff Thompson: Well, and…and again, this is…

Vyn Reese: …and we need to make sure we keep updating on all these classes, because things change quickly.

Jeff Thompson: So…so this is…though, I absolutely agree with you, Vyn, that we'd have to be smarter about how we do our off-label sort of analysis guidelines and restrictions. This is totally about feedback.

Vyn Reese: Okay.

Jeff Thompson: This is totally about just telling you, "How do you compare in a statistical analysis to your peers?" And so the way the Dear Prescriber letters look is that…and in this case, you'll see Dr. D. Well, you know, and how do you compare, say, in one particular class, this would be cholesterol lowering, you have over the last two quarters 22 or 23% generic utilization. Your peer…again, pediatric, primary care, and mental health, nurse practitioner or other…they have, you know, somewhere around 47 to 49%. And then compared to a best practice…and a best practice would be the top quartile, so that the top 25%, how do they compare in statin utilization? And so that's the type of analysis…and we've done one round. The second round will come out here…actually, I think it's coming out right now in this…next couple weeks. And then we'll also compare you and your DAW utilization. So how often do you use DAW compared to your peers, same peers, or that best practice, the top quartile? And so you have an example of one the letters there. Yes?

Carol Cordy: This is Carol Cordy. You...these are just going to that 800 and…

Jeff Thompson: These are just going to that 824.

Carol Cordy: And that's a cost…I mean, it seems like this would be helpful for everybody to get.

Jeff Thompson: You're absolutely right, and so what we're…what we're going to do is do…just get a couple rounds of this and figure out it's…if it is effective, and then hopefully what we'll be able to do is then generate these electronically, post them for somebody to actually go on a website and look that their…look at their analysis. Well, we're working with Duane and Ray. We might even be able to post it on the RX.WA.GOV where you could go in and update your endorsing status but also look at your prescribing. But I think before we do 15,000 reports, let's start out and understand the nuances with doing these reports. Is this the correct definition? Is this the correct way of actually giving you this information? Is it useful? Is it timely? You know, and from those learnings then I think we can probably get bigger.

Carol Cordy: Just because we're all competitive people, and…and want [inaudible]?

Jeff Thompson: Well…

Patti Varley: Can I ask a question?

Jeff Thompson: Sure.

Patti Varley: When you look at that and you have the payers, is that in a similar type setting? Have you looked at tertiary care versus primary care comparisons, or is this?

Jeff Thompson: So…so we did not…we did not tertiary versus primary care. We did not look at that. What I figured is, possibly naively, is that because we're only doing six drugs classes with a lot of generic options, and within those six classes when you look at Generic News, there's no difference between brand and generic that there should not be mine are…the issue of mine are sicker, you know, mine are different when you…when you restrict it to this type of classes. Now that said…there are obviously nuances…hold on….so…so the comments we're getting back now on the feedback reports is my clients come in on brands so I can't really affect that brand utilization. Mine are sicker. I see…I see the people that are allergic to the blue pill, and I need to prescribe the red pill only. Wrong peer group, and so we're giving the options of people to change their peer grouping, because, you know, obviously we can only look at and make assumptions about whether your primary care pediatric, you know, mental health, ARNP…that's an easy one. A little bit more…but…and then other. And then the other is interesting. I should only be, you know, compared to a gastroenterologists in and around my area and that's it, which I don't believe is true with…again, with these classes. A lot of people say, can you send me my full profile, so we're making that available. If you want to see all your prescriptions, our contractor that's doing this will send a full prescription profile when I get a letter. It is enlightening, because a lot of people say, I always write for generics, and so I really believe those pharmacists are prescribing brands…so we're working that angle…and then…and then they also…

Patti Varley: Does that happen?

Jeff Thompson: I don't believe so, but that's the perception. And then…and then my colleagues are writing for all these, and I'm just writing the prescriptions for my colleagues.

Siri Childs: Can I comment on that?

Jeff Thompson: So these are…so these are the comments that are coming back. Go ahead?

Siri Childs: You know…this is Siri. There are some cases where a retail pharmacy will get a brand at a low cost, and the best example of that is Deltazone for prednisone, but they are supposed to be indicated…indicating a 5N when they run the claim so that the payers know that they are submitting a brand, and it's acceptable to give them the mat cost on that.

Jeff Thompson: So I think there are probably rare exceptions where those were happening, but likely not in these drug classes, because they're fairly established, but I'm chasing those down. And I think it's just as important as doing education about perception of what's real and not real, so everybody's getting a standard letter back and where I need to, you know, I investigate and take a look at them, and then our contractor, HWT, actually will actually talk with the provider, share their prescription information. Out of the 824, I think we're up to like maybe 60 or 70. You know, it's actually less than 10% have actually given us feedback with letters and concerns, and so I think on the second round…and you have an example where there will…they will see not only their trend from quarter to quarter on their brand, generic, and DAW, but they'll see both, you know, whether they're account of clients have gone up, their account of prescriptions have gone up or down, or you know, and what has been the delta difference in their spend between brand and generic. All that is produced on a table, and so that…so just now we'll be starting, you know, two points on a curve, and…and then just to finish up where we started.

In 5892, I will…we will give them three quarters of information before they'll be any action taken. No action will be taken unless there's a consultation with my office. If they can substantiate why brands are more effective then generics and their practice for whatever reason, red pill, blue pill, you know, then…then they'll be no…they'll be no…no foul, no harm. But if…if the case is after three quarters there is no statistical difference in their prescribing and they cannot explain why their DAW and their brand utilization is so high, 5892 allows me then to ignore their DAW in Medicaid. I'm hopeful that that will not happen. I'm hopeful that they'll be at least explanations, if not a good trend towards more generic and less DAW utilization, but we'll have to see, and that won't happen until likely late…late spring, early summer. So that's the early

statistics. That's the process—about as open and transparent as we possibly can. I'm hopeful that these feedback reports will be informational, and I'd love to hear back from you about whether this is too much, too complex, not enough, whatever, and any other things that Siri and I and…and group can do. Yeah, Barak?

Barak Gaster: Yeah, so…Barak Gaster…so I've got four suggestions for making this a little bit more user friendly, and I would first say that having a little footnote at the bottom that defines what best practice means, having a little footnote at the bottom that defines what your peers means. I would suggest keeping the Y axis consistent among the graphs so that you can compare among the drug classes by the size of the bars. And then I would attach a table that lists for doctors what drugs are available as generics. I would say that one of the biggest problems that exist in our health care system today is that drugs go generic, and it's almost impossible for physicians to find that out. You know, it's always this constant sort of looking a drug up on Drugstore.com to see if a generic is available or not, and so I would think that…that a…at least one piece of the puzzle is better educating doctors as to what drugs are available as generics and what aren't, especially as Vyn said a minute ago, this is changing so quickly. So many drugs are going generic so quickly, and it's really hard for physicians to keep track of that.

Jeff Thompson: Right, and I agree with you with the generics, and in the next generation of Generic News, we will point that out. I would point out, however, generic substitution makes it so you don't even have to think about it. If you write for the brand and you don't write DAW, the pharmacist will automatically dispense the generics. And so trying to keep up on that is, you know, and especially when you look at the NSAID drug class and there's 60 drugs in there, so I…but…so I would push back that there is a conscious decision by writing DAW to utilize the brand over the generic, because all you have to do is passively write the brand name which has been ingrained in your head over that period of time. It will automatically be substituted.

Barak Gaster: But I would say that there is so much ignorance out there that people are writing for not…are…are writing for brand names, not DAW, but for drugs that are only available by brand, not realizing that there is a almost identical drug too that is available generically.

Jeff Thompson: And…and we'll…we'll…we'll put that out in Generic News.

Patti Varley: So this is Patti Varley, and for me that…a concrete example would be Ritalin LA, even if you put, may substitute, they wouldn't necessarily put medidate CD. So that is an example, I think, of what Barak's talking about. I have a question too about on this handout, the second page…

Jeff Thompson: Hm mm.

Patti Varley: When it says, generic utilization like 47% and DAW 19%, that doesn't add up to 100. It's the…it's the letter…the example letter going out to practitioners.

Jeff Thompson: I'm just trying to…just trying to think about how your…your DAW and your brand would not be equal, and you might have a different distribution in a drug class.

Patti Varley: Well, but they…this makes it difficult…so if your DAW is 19%...

Jeff Thompson: Right.

Patti Varley: …and your generic is 47%, it looks like you're doing more generic than you are DAW, but your peers are doing 66 and 9. Well, my math says 66 and 9 is 75, and 47 and 19 is 66…

Jeff Thompson: Well, remember…well, remember you're talking about two different metrics, so D…

Patti Varley: But they're on the same chart?

Jeff Thompson: Right, but DAW does not equal generic utilization or brand utilization 100% of the time; and because it's an…it's a mix of six different drugs classes in your generic utilization and your DAW utilization, you're not going to have a one-to-one relationship.

Patti Varley: So I…I guess I don't know how to…

Male: Like for example, Crestor preferred, so you don't have to DAW to get that, and that's a brand.

Jeff Thompson: Right. So you could…you could…you made several motions today where, you know, we could include a brand as a preferred with generics, and therefore your DAW wouldn't apply to that brand. Your question would only be applicable if all of our preferred drug list was generic only, and the only way that you could get a brand was to write DAW. And in this…and in…in these classes, there…there are some brands that are available. ADHD for example, you want…you want the long-acting brands to be available in both drug classes. So DAW does not automatically equal, you know, all brands or all generics. Does that make sense?

Patti Varley: That's okay. I'll…

Siri Childs: If we said that one column was brand utilization, and one column was generic utilization, and those two would total 100%, but Jeff is not saying that he's saying percent generic use, but he's saying percent DAW.

Jeff Thompson: DAW and brand utilization would be equivalent…

Patti Varley: Only if…

Jeff Thompson: Only if.

Patti Varley: Right. I got it. Yes.

Jeff Thompson: Okay.

Carol Cordy: I have a couple questions…Carol Cordy…who…who does this Generic News go to?

Jeff Thompson: I have given that to all the associations. It's sent out in all the letters to the 824 and offered the Generic News to anybody that wants to push it out…

Carol Cordy: Okay.

Jeff Thompson: …in the associations.

Carol Cordy: And then my other question on the daily…the average daily cost ratios...

Jeff Thompson: Right.

Carol Cordy: On the…all these drugs. Is that based on the…the deals that DSHS makes with this?

Jeff Thompson: So…so the average daily cost is our net cost on the preferred drug list which is all three agencies, included supplementals and discounts times your utilization, times your…how much you prescribe, that…and then put as a ratio from low to high.

Carol Cordy: Okay.

Jeff Thompson: So it is the net cost to all three agencies, but it includes your prescribing, because that's one of the additional elements that's never really included. So let's say we get the best drug price on the 10 mg but you always prescribe, you know, you know, the 20 mg, you know, 12 pills twice a day, so it doesn't…

Carol Cordy: That's factored in there?

Jeff Thompson: Yeah. That…so that factors in your prescribing in the average daily cost, so it's our net cost as a collective three agencies times your average prescribing for that drug class, that pill, and that…and then what you do is you take a ratio of the low to the high so the lowest becomes the denominator, and then everything is…is divided by that lowest.

Carol Cordy: So and I guess…I mean, one of the reasons I ask that is if I were to get this, this would have nothing to do with what my patients who don't have coupon…who don't have medical coupons.

Jeff Thompson: Well, one of the reasons…

Carol Cordy: …we find in the pharmacy.

Jeff Thompson: …why we can't make this Medicaid specific is there is a possibility that you could back calculate what each manufacturer's supplemental rebates are so we cannot make this specific to just Medicaid. It has to be all three agencies.

Carol Cordy: All three? But…but still it…it wouldn't apply to anybody else?

Jeff Thompson: Well, I would say I've looked at….I've looked at most of the other formularies and things like that. You know, within a factor of let's say, you know, 10, 15, 20%, these ratios still apply. Generics are always cheaper than brand.

Carol Cordy: Right.

Jeff Thompson: Brands never come down in cost compared to generics. As a matter of fact, generics are going down in cost nationally and brands are going up in cost, so the ratios…they might, you know…let's say, if you compare us to Group Health, you know, item 5 might be switched for item 3. I mean, they might go up and down, but…but…but pretty much it all looks the same. When we look across uniform medical, L&I, and Medicaid…Donna correct me, Siri correct…there…you know, sometimes you might swap a space or two, but they're not radically different. It's a rare occasion when they're radically different and cost…and average daily cost.

Siri Childs: This is Siri. With all of our drug manufacturers sitting here, I really do feel like we need to clarify one of your statements when you said that generics are always cheaper, because you know…

Jeff Thompson: There is one…there is one exception to generics are cheaper. During the six-month exclusion where a generic manufacturer who is so brave to put their generics out first, the…the deal with the federal government is that they can have exclusive rights and price whatever they want for those six months, and they are typically at or near brand utilization costs. After six months when multisource come in, it drops like a rock when…when the second, third, fourth, fifth prescr…manufacturer comes in. So that is the only exception to the principle rule, algorithm, whatever, that generics are cheaper.

Barak Gaster: Call it generalization.

Jeff Thompson: Generalization. And…and just…and just the further nuance with that is it…it is impossible for Medicaid to take advantage of…of special deals, because we would have to go against the state law for generic substitution. So a special deal for Medicaid during that six-months exclusion, than I would have to communicate to every pharmacists but only for Medicaid only, because every other formulary, every other PBM, is trying to put the

generic in, in place of the brand. So that's one of the difficulties of special deals. You either play generic substitution or you play supplemental rebates, but trying to mix the two gets very difficult.

Vyn Reese: And…and Jeff, again…again, this is Vyn. I remember when Zoloft went to generic to Sertraline and for a…some strange reason Sertraline was not on the straight formulary even though it was a generic, and I was writing for Sertraline having it denied, even though it was a generic. So we've got to be sure…I mean, as I just gave the other instant of Gabapentin that we keep up to date as to what is generic; and when it goes generic, we can write it as dispensed…you know, as…don't write dispensed as written but just please substitute and actually be able to get the prescription, because this is…this is a rapidly moving target, and these drugs are changing all the time. And every time that happens, I lose confidence that you're keeping up. Okay? That's my concern.

Siri Childs: This is Siri, and I'd like to respond to that, because before Senate Bill 5892, we went with our drug reviews on a quarterly schedule, and that…we updated quarterly based on, you know, your reviews. But with Senate Bill 5892, we now are allowed to put generics on the PDL without coming to you first.

Vyn Reese: Right. Okay.

Siri Childs: And so now as of July 2009, you should probably have seen us already in action where we slip the generics in just as soon as they are available.

Vyn Reese: Great. That's a huge improvement.

Siri Childs: Mm hm. But that was 5892 that allowed us to do that.

Vyn Reese: Good. Okay. That's excellent, and that answered my question.

Jeff Thompson: So…but I agree with…I mean, we'll do…we'll…the footnotes on best practice, what does that mean, peer grouping, looking at trying to keep the graphs consistent. I remember going back and forth with the contractor on that, so…and then…and then talking about, you know, which generics are coming on, and that's why we'll produce another Generic News…we'll try and do this on a quarterly basis.

Barak Gaster: Yeah. This is Barak again, and I would say…I mean, the Generic News…newsletter is great. There's a lot of good stuff in there. I would say that it would be very useful to have a separate table that was an attachment to the report card that just simply listed what drugs are available as generic. So sort of boil it down to less information…so take out the average daily costs and the annual days supplied and take out the three or four paragraphs that are…go with each class, which is useful for somebody who's motivated enough to read a newsletter. But if you just…if you would just attach it as a…as a short attachment…

Jeff Thompson: So you're saying 6th grade education level to our prescribers out there?

Barak Gaster: Absolutely.

Jeff Thompson: Okay. Got it.

Barak Gaster: Absolutely. And also don't overestimate how well doctors know what generic name goes with what brand name. And so I think that the list should…the list of drugs available as generic should include in parenthesis what the brand name is so that physicians can immediately recognize what drug you're talking about.

Jeff Thompson: Well, just so you know the complexity. I mean, this took a lot to get down to this level. If you look at the NSAIDs and look at your choices…

Barak Gaster: Yeah.

Jeff Thompson: …in listing both brand and generic…

Barak Gaster: Yeah. So I mean, so then maybe…

Jeff Thompson: …it starts…it starts to get pretty [inaudible].

Barak Gaster: Right. So maybe NSAIDs is not…is not the right class to be using for this. I mean, but I think if you did that for the other classes…

Vyn Reese: In all…

Barak Gaster: In…in…because you're trying to…you're trying to affect behavior change in people who are really busy and only vaguely interested, and so the more

sort of immediate tools that you can give people to change their behavior, the better able you'll be to do it.

Jeff Thompson: And again, these…these six drug classes minus the antipsychotics represents our top six drug classes and our spend. So if you just…if you just rank order drug classes, these are the…these are the top six out of seven minus antipsychotics which is a quarter of our entire budget.

Barak Gaster: And let me ask, so in this way in some ways NSAIDs may not be the lowest hanging fruit, because it has had the least movement among these six classes of recent generics, so it's you're least likely to get at physicians who are just not aware of newly generic drugs in that class?

Jeff Thompson: The only thing I would point out to you in NSAIDs with all your deliberations, we still have…you can see where Celebrex is…

Barak Gaster: Yeah.

Jeff Thompson: …on the list?

Barak Gaster: Yeah. But that…that's complicated by so much marketing and theoretical advantages.

Jeff Thompson: I'm only trying to communicate your…your…this is all you guys. On the left side, this is you. Well, you want me…you want me to get rid of you?

Barak Gaster: For…you…you need a different level of communication.

Jeff Thompson: Okay, because…

Vyn Reese: Well, and…and I agree with Barak. I think that…this is Dr. Reese…that keep it simple, stupid is…applies to doctors too, because you don't…yeah, you're so busy, you want to…if you have a really powerful message, you want to keep it simple, keep it what the doctor's actually…uh hah…these are…this is now generic. I'll now prescribe it. I mean, just keep it to the drugs you really need to have them prescribe in each class.

Jeff Thompson: And I thought they wanted the evidence.

Vyn Reese: Well, they do want the evidence too, but they want to make sure they know what they can get away with writing without getting dinged, you know. I mean…I mean, because if you get a call from…and it's…you have to call the pharmacist and fight with them for the drug, that's a real disincentive, but it's…that's…then you get mad at the pharmacist and you get mad at the State and get…have all these things that are upsetting. But if you know what's generic and each class, then you have only yourself to blame if you don't do it. It's just right in front of you. And as things…as things become generic, we need to make sure we educate providers. It'd be nice to even have some little tiny card that had the generics on it or some little thing you could put in your pocket or something that just had a generic list that…that would be easy to look at and refer to. A lot…a lot of the other, you know, the big…of course, some of these are very complicated formularies, but they try to…they usually, you know, dispense those quarterly, and all the big pharmacy companies that are…that are associated with insurance companies will distribute those, so you'll see what's generic and what's cheaper.

Barak Gaster: And this is Barak again.

Jeff Thompson: I can…I can say that Siri and I have…have gone out to the healthy options plans, and we've…we've talked with them at length, especially with the mental health drugs…can say that our mental health preferred drug list and our formularies in…in healthy options are almost 99% similar, and they were…they only actually deviated by one or two drugs, you know, in one class. And so we've really worked hard to try and get to that similarities with…with the formularies and preferred drugs and we can start looking at the other ones too.

Barak Gaster: This is Barak again. What…I mean, what you want to be doing is you want to be sort of piggy backing, coat tailing on the incredibly effective marketing detailing that has gone on in the past 10 years. And so…

Jeff Thompson: I don't have that kind of money.

Barak Gaster: No, you can. You can. All you got is…so doctors have just…you know, so many doctors have been…had it drummed into their heads that Celexa is the best antidepressant, and you know, they now just need to know that it's generic and…there you go.

Siri Childs: This is Siri, and I want to address a comment that Dr. Reese made about listing the generics. If you go onto the pharmacy website for Medicaid, I have in my hand the way we present the preferred drug list, and it lists all the generics first that are preferred and then the brands that may be preferred, but then we list everything generic and brand that is nonpreferred.

Vyn Reese: Right.

Siri Childs: So have a list already made for you if you go on our website.

Vyn Reese: And that's the thing.

Siri Childs: Yeah.

Vyn Reese: If you…they're not going to go to the website. They're not…they're too busy to do it.

Jeff Thompson: Well, again, just…I mean, just not to push back, but I think, you know, generic substitution works. Within the first month when a generic comes on, 95% of that brand goes away, and generics get pushed across the counter, unless you write DAW. So there is, I think, a majority of active component in prescribing brands, at least in these 824 over just naively not knowing the difference between brand and generic.

Barak Gaster: Right.

Jeff Thompson: They…they have to write…if there's a generic that's equivalent, they have to write DAW to get the brand.

Barak Gaster: But so…I mean, physicians have in their mind that Fluoxetine is an old drug, and it's…you know, it's not as good as all of the newer drugs, and so then they got…they got detailed heavily 10 years ago to switch to Celexa, and so then they used Celexa for a while and had in their minds that Celexa was a much better drug. But then since then, they got detailed heavily and switched to Lexapro, and they left Celexa behind, because Lexapro is even newer and better. And so now if you can push it into their face and say, you know, actually Celexa, that drug that just a few years ago you thought was the cats pajamas is now available as a generic, they'll say, oh, gee, maybe Celexa is about as good as Lexapro, and they're both

all much better than that old drug Fluoxetine. Maybe I'll start switching to Celexa, and gee, I don't even know what that brand…or the…what that generic name is. So you just give Citalopram on a list, they won't even recognize that as Celexa.

Jeff Thompson: So…so I would like to challenge the group that I would be more than happy to…I will send out another one, but a letter from you that is two paragraphs to the point that you want to make, signed by all you as representatives of the community prescribers, I think, would be very powerful, because you know that Jeff Thompson pointy headed bureaucrat, you know, he's just trying to make trouble out there. So I want to…I want to offer up to you that, you know…and I'll…I'll even write it and you can edit it.

Vyn Reese: Sure.

Jeff Thompson: But I think….I think, you know, you are the representatives of the prescribing community; and if I'm not hitting the mark right, you know, I…I will edit…let you edit it, but I would like, you know, if you could sign it, I think that would be a very powerful statement to the prescribers out there.

Vyn Reese: Jeff, this is Dr. Reese. I'd like to sign it.

Jeff Thompson: Yeah. Okay.

Vyn Reese: I have no problem with it. I think it's a good offering, and I think we're just giving you ways to…

Jeff Thompson: Sure.

Vyn Reese: …I think can improve it. I mean, we…we're totally behind…at least I'm totally behind this. I'll be happy to sign a…as long as I have edit, you know, capabilities, you know.

Jeff Thompson: You'll get it…you'll get it…

Vyn Reese: You're usually a pretty good writer, though.

Jeff Thompson: You'll get it next week.

Vyn Reese: Okay.

Jeff Thompson: Okay? And then that will go out in the…the next generation, and it will include, I think, Barak…that was in the next…we…we do need to communicate better brand versus generic, and so Siri and I will work on that. We'll get a nice clean sheet just for these six, and then point it back to RX.WA.GOV and then our website.

Carol Cordy: This is Carol Cordy. The other thing that might…you might throw in next time is talking a little bit about H2 blockers instead of PPIs.

Jeff Thompson: Sure.

Carol Cordy: Which the State has kind of done, but what if…

Jeff Thompson: We'll actually be putting the generic first initiative which includes the PPIs, H2 blockers and those all in here to kind of explain what's been going on and the why. That's good. Yeah.

Jason Iltz: Jeff, this is Jason. Just a couple quick little things, and maybe it's just what you said, but as I look through these lists, I think something that would get to Barak's point is simply putting the little trademark symbols on the list itself next to branded medications. And then the other thing would be, you know, even the…the PPIs is the shortest list, and it has what, 10…10 different things on there. By the time I get to the bottom of that, I really kind of forgot what the top three were, or top two, or whatever it may be. So you know, I'll leave it to your discretion, but maybe you want to bold that cheapest one, that really has shown that, you know, there…it's…in most people, that's a good place to start. And so maybe you want to bold that top one or bold the top two, or however you want to do it, but I think that would at least draw the attention back to, hey, in this class, here's the cheapest one and maybe that'll stick a little bit better from that standpoint as they move forward.

Jeff Thompson: I wanted to ask a question. As you look through the average daily cost, are you at all surprised or shocked or is it not surprise, not shock, at the differential and the cost between the lowest and the highest? I mean that was something that we came up with as a group as the only way that I know of to give you cost information without disclosing, you know,

rebates. So this is…with all the rebates, with all the supplementals and federal and the discounts given to all the PBMs, this is the net.

Alvin Goo: Jeff, this is Alvin. Again, I think your generic letter is excellent, but on…I just wanted to clarify on the average daily cost ratios on page seven, the differences between Wellbutrin…

Jeff Thompson: You picked up on that one?

Alvin Goo: And…and Bupropion XL, what…I understand that.

Jeff Thompson: That was…that was the exception. That was the six-month exclusivity.

Alvin Goo: Oh, okay.

Jeff Thompson: During the period that we caught that, that average daily cost, you win the door prize. Very few people picked that up, but…but that was during that…that six-months exclusivity that was the exception. And I've had…

Alvin Goo: That…

Jeff Thompson: …two providers out of the 824 that picked up on that.

Alvin Goo: But has that since changed, or is it still the same?

Jeff Thompson: It…it has changed.

Alvin Goo: Oh, okay.

Jeff Thompson: Yes. It has changed, and in the next go around, I can present these tables again on an annual basis as we go through the cost analysis. But in general, nationally, generic costs are going down, brand costs are going up, so the ratios as you see them there, at least nationally, are going in opposite directions.

Jeff Graham: This is Jeff Graham. I'm just sitting here as an observer, but I heard some of these folks say up here, this is too much information. We don't need all this ADC and the comparison. We just need to know what the generics are and what their brand name was, or still is, and…and then maybe just a comparison down in the list, but we don't need all of this.

Jeff Thompson: So just so you know…

Jeff Graham: ADC and so forth. Now, maybe they didn't all say that, but I'm just wanting to make sure they clearly tell you what they really want, because I've heard conflicting opinions here.

Jeff Thompson: So the issue that I have is you are…you are the worried well. The 824 are the uninitiative, and uninitiated. They asked for this information, because they believe that brands are less expensive than generics, and so I have to give…I have to give them, you know, a limited amount of information. So, you know, anytime you do communication, you know, you're shooting for a middle, but I think these are excellent suggestions that, for the next generation, we will make it simpler.

Patti Varley: Well, this is Patti Varley. I think that that would be helpful. I think that there's always the people who want more than…than…

Jeff Thompson: Right.

Patti Varley: So referencing how they would get there is okay? You know, like if you, you know, having this posted and making a reference that if they want to…if that is that person who's going to read it all and not need the highlight in their face, that you can refer to if you want more information.

Janet Kelly: This is Janet Kelly. I actually think that, you know, the average daily cost…I don't really care what it is, but the difference between $1.00 and $55.00 kind of does say something. The part I don't understand is…

Jeff Thompson: And it's not dollars. It's a ratio.

Janet Kelly: Okay. That ratio there. I mean, that's…

Jeff Thompson: In the footnote, yeah.

Janet Kelly: Yeah. Oh, if it could be a penny, I guess it doesn't matter.

Jeff Thompson: Well, actually when you're doing a million prescriptions or…

Vyn Reese: It's a lot of money.

Jeff Thompson: Or a million month.

Janet Kelly: I didn't understand the second column. Now, I need to use the second column to figure….

Jeff Thompson: Right.

Janet Kelly: Okay. Now, I get it. I'm a little slower.

Barak Gaster: Jeff…

Man: [inaudible] (no microphone)

Jeff Thompson: It's the ratio of the lowest to highest. Not a cost, down the footnote. So you take the average daily cost net times the average prescriptions, the number of prescriptions dosages written. So that's your average daily cost, and then you basically divide the lowest to each one of the drugs, and you come up with a ratio, an average daily cost ratio. So all you can say is that if the lowest cost drug is one and the next one is five, then that brand is five times more expensive than the generic. Now, that generic might be priced at two cents, and so then the brand might be then five times more, or the generic might be $1.00 a day, and the brand is $5.00 a day. But because we are restricted from producing data where it would disclose the rebates, I have used the average daily cost ratio. So it's a ratio not a dollar value.

Jason Iltz: This is Jason. Think of it as an odds ratio. That'll…I mean, seriously, I mean, that's really what he's done, but it's on a cost.

Nate Miles: [inaudible] you're looking at it, and you…having to going through that and sitting here, you're a doctor [inaudible] prescribe [inaudible] cost $1.00 and another one that might cost $30.00.

Jeff Thompson: Right.

Nate Miles: Because it's a ratio. So you don't…you certainly don't want to spend $30.00 when that might not be the case. That's not even close to [inaudible].

Jeff Thompson: So I think the question you should ask is are you getting thirty times more the value, or are you getting five times more the clinical value? I mean, Nate, this is trying to get at what you've always preached to me is are, you know, what is the value equation, and so this is about as transparent as I can make it.

Nate Miles: Which was going to be the next question in this. It seems like that's the questions about how a drug turns out and the success that you have. Shouldn't there be a question in here somewhere about such as switches and everything that have taken place? What have the doctors also found in patient care? Has patient care gone up? Has quality of care gone up? Has adverse impacts gone up? Some of that other information that goes along with patient care that we need…talking about are the things of some of that, so that the doctors use this as a prescribing tool, one of the tools in the toolbox. They also have some guidance as to how things have been going from a patient care standpoint.

Jeff Thompson: Sure. We can add that.

Nate Miles: Can you get that in there?

Jeff Thompson: We can…as…as we get…this is the first edition. So on the left-hand side where basically was distilled down your information here, and OSHU used 900 pages down to a paragraph or two, we can include, you know, data from like the NSAIDs where one of the reasons why we deny access to NSAIDs for people that have had a GI bleed in the past, is we did an analysis that you are more likely than to actually bleed again if you give an NSAID, and we can…we can produce that…that analysis in a…in a study done by OSHU on Medicaid clients. Yes?

Carol Cordy: This is Carol Cordy again. I think there still needs some kind of a disclaimer for people that really need this.

Jeff Thompson: You guys are…you guys are tearing apart my baby here.

Carol Cordy: No, no. No, just those two asterisks that really kind of says this cost ratio does not apply to, you know, what goes on out there in the real world.

Jeff Thompson: Well, no.

Man: This is the real world.

Carol Cordy: No, well, but I mean what goes…this cost ratio is based on what Medicaid and the…

Jeff Thompson: No, no. This is all three agencies.

Carol Cordy: No…no, I know that.

Jeff Thompson: So this is…this will look no different than Group Health, Premara, or Regence.

Vyn Reese: And Jeff does do that on the bottom of the NSAID. He does do the monthly cost per brand versus the generic monthly cost for NSAIDs. It's a huge difference.

Carol Cordy: Yeah, right.

Vyn Reese: I mean, that's really good.

Donna Sullivan: [inaudible] and then the ratios is not. I looked at the bold thing at the bottom and it says monthly cost brand. So I took this to mean these were dollars. So I think that…it's reading carefully but…I mean it's there it's just a matter…the little tiny note is very tiny and the big bold of dollars is what your eye focuses to.

Jeff Thompson: Actually, now that I notice that the actual…in this version, the little footnote got cut off on two of them, so.

Man: Okay.

Carol Cordy: It's really good. It's all really good.

Jeff Thompson: I try. So I'll have something…Siri and I will work on something, a couple paragraphs, perfect five-sentence paragraphs, for your editing, and then…and we can get it with the next for all your signatures.

Vyn Reese: Good. Thank you, Jeff.

Jeff Thompson: All right.

Jason Iltz: Question. This is Jason. On House Bill 5892, does it mandate the use of generics when a prescription is written for the brand name? Let's give an example like MS Contin, for example, but the prescriber signs substitution permitted, does the House Bill say that substitution is required in that case? And I'm asking the…

Male: [inaudible]

Jason Iltz: And I'm asking the question…and we don't even have to have an answer to that today, but it's something to think about as we move forward in this, because not only the prescriber's very important in this communication, but there's a lot of patient preference for certain classes of medications, pain being one of them. Opiates being one of them. So at the level of the patient, there's a lot of times they will come in, and if it says, MS Contin, and even though it's written substation permitted, doesn't say substitution required. They will request that it be filled with MS Contin as opposed to a cheaper generic alternative. And so what needs to happen or is there something in the House Bill that the pharmacists need to understand and say, look, you have to legally substitute it unless there's a real reason why they can't have that generic.

Jeff Graham: This is Jeff Graham. That's a poor example. That's a class 2 drug, and you cannot substitute those. It has to be a written prescription.

Siri Childs: But I would like to respond to that example. This is Siri, and for Medicaid, if…if the physician has written substitution permitted for a brand, even if it's MS Contin, then we are going to insist that we will only pay for the generic for Medicaid.

Donna Sullivan: Jason, this is Donna Sullivan. Jeff, just as a correction, yes, you can make a generic substation for a C2 drug if the doctor allows substitution without having to get a new prescription. Jason, to your point, if the doctor writes dispense as written on a product that has a generic available, the generic substitution laws still apply, and the pharmacists is required to dispense the generic unless the patient says, no, I want the brand. So for Medicaid, I heard Siri say that they would not allow that or they would only pay the pharmacy as much as they would pay for the generic even if they gave the brand. For Uniform Medical Plan, it's…we allow the brand to be dispensed, but the patient pays a higher cost share.

Jeff Thompson: Right. Right.

Donna Sullivan: The bill itself doesn't require substitution for the…for the…what? I forget the name of it. 5872 or whatever? But generic substitution laws still apply despite the new bill.

Duane Thurman: This is Duane, just to add. It really does not relate to 5892. In that situation, it's really a question of generic substitution, and the summary is Medicaid will pay for the generic UMP. I can choose to pay out of pocket and get what I want.

Patti Varley: So…this is Patti Varley, and because we had this…I'm just again wanting to clarify that I understand if you write for a brand name and you say, may substitute, but the generic would be substituted, the question, because it came up and it had to do with…

Woman: [inaudible]

Patti Varley: Right. In the times where manufacturing of controlled substances is such that access to one or the other, how does that play out in regard to, for instance, may substitute but the generic…the pharmacy only has brand name, doesn't have generic, how is that going to play out? Because my guess is, you know, this was one example, but it's going to happen again, and there will be other times the pharmacy only has something in supply. Just because I think that the ease of the symptom, that wasn't an ease in the symptom. I mean, many of us were trying to be compliant, and then we ended up having to rewrite prescription, and you know, phone calls and discussions with pharmacies, and that becomes less appealing. So then people I know started just signing DAW for it, because they didn't want to be bugged anymore. So when the generic became available, they were still DAWing because it was such a hassle.

Jeff Thompson: Well, I think you're right, and the communication we can about. I mean, the issue is is that we can't drive the whole program by the exceptions. I mean, those are exceptions, but they are headaches. I think what we need to do is to Barak's thing, tell people that things are going to go generic, maybe give them notification ahead of time. Usually during the first two to three months, these type of headaches can occur because of supply and

demand and…and just to, you know, sort of bear with it and it will smooth out over time.

Patti Varley: But there isn't…there is not a way…I guess, I'm confused by if I write Focalin and I say, may substitute, it can be substituted with D-methylphenidate. But if I write Focalin and may substitute and there's…and they only have Focalin, they won't fill it for Focalin. That was the part that was confusing to me.

Siri Childs: They won't fill it for Focalin?

Patti Varley: Unless they got a new one that said DAW. That's been my whole point.

Vyn Reese: The pharmacy didn't understand it.

Patti Varley: And…but that was multiple. I mean, that's where I got nervous, because people started to write DAW again, because they were harassed about rewriting prescriptions, and patients weren't getting their meds, and I don't understand if you can do it that way, why can't you do it the other way? If you can…if you can do the sub…if you can do the generic for the brand, why can't you do the brand for the generic if you don't have the generic?

Siri Childs: I think you can.

Vyn Reese: This is Dr. Reese…it should be…if it's AB rated, they should do it, and maybe there was a confusion on the pharmacy's part. What happened was I was writing when Oxycodone LA was available, I wrote for Oxycodone LA, and I'd have patients getting OxyContin, because there wasn't any Oxycodone LA because it all got…it all got recalled.

Jeff Thompson: So I think these are examples of the exceptions that we remember in our mind. Remember, Medicaid fills a million scripts per month. We're talking about…how many?

Patti Varley: But they're the ones we hear about.

Vyn Reese: They are the ones we remember, right?

Carol Cordy: And this is Carol, again.

Jeff Thompson: Carol, I think is it incumbent on us to basically let the prescribing community know that when there is…when there is a generic that will come on that market, we pretty much know, you know, ahead of time, sometimes not as much as we like, we can try and figure out how to say, there may be some disruptions in the market. Here's the process, blah, blah, blah. We can…there's a certain statin that's going to go generic at some point in time, and I'm sure that'll be problematic too, so.

Carol Cordy: Okay. I just want to clarify it seems like, because it's happened to me maybe 10 times, where I can over the phone without writing a prescription just say, oh, do DAW, and then it…I don't have to write another prescription.

Patti Varley: Correct. But that is not consistent.

Carol Cordy: Is that typical?

Patti Varley: Yeah. And the question is, is that…because some will allow you to be able to say, yes, just say I said DAW. Others will say, no, I need a new a prescription that says DAW. You can't fax it. The family has to come to get it or they have to have it mailed to them.

Carol Cordy: But from your perspective, we can over the phone say, DAW?

Jeff Thompson: You typically can, and the only place where it gets to be problematic is when you're in the…the C2, C3 classes.

Donna Sullivan: This is Donna Sullivan. I think that the question is what you're running up against is whether or not it's…the pharmacist is legally able to, under our current laws, to do what you're talking about, and I think that they are. The question then is, it's that individual pharmacy's policy to not allow the pharmacist to do that for most likely audit reasons. If they get an…they get audited and a prescription originally didn't have a DAW on it, then they're concerned about an audit where they would get their money taken away from them so they're requiring you to provide a new prescription instead of them just writing a note on there that they talked to you, who they talked to, what time and date and got the order, so.

Patti Varley: Well, and now with the new tamper proof, you're…you're not allowed to cross out, initial, and sign on the other side either, because you're so…not supposed to make any corrections on the tamper resistant prescription.

Jeff Thompson: Right. But I…but I…

Donna Sullivan: And that could be what's driving them right now.

Jeff Thompson: But I will point out to you that pharmacists, and you can correct me if I'm wrong over there on…in many of the retail pharmacies on a day-to-day basis, electronically they are being tracked on a prescription by prescription about what they're prescribing is…or what their dispensing is, I should say, and what their brand and generics and what the profit margins are, that is actually on a prescription-by-prescription basis. We're trying to get that same type of information out to the prescribing community. Because if we can be more efficient and effective in our $400 or $500 million spend, perhaps there opportunity to buy back the basic health plan, the GAU program, etc., etc. But without this kind of information, with corrections and editing and blah, blah, blah, we are indiscriminately wasteful in my opinion.

Vyn Reese: Nobody disagrees with that.

Jeff Thompson: Okay.

Vyn Reese: Nobody disagrees with that.

Jeff Thompson: Okay.

Vyn Reese: Okay. We all are…we all agree. It's wasteful not to prescribe…

Jeff Thompson: Just want to get that on the transcripts if read by others, that's it.

Vyn Reese: No. If you don't prescribe a generic and there's a generic that's equally good in the class, you're wasting the State's money and taxpayer's money, and it should be everybody is aware of that. And if anybody doesn't look at that and see that, then they're…they're not very bright or they have another interest.

Jeff Thompson: And I have a list of physicians here, anybody, you know, if you'd like to make any phone calls. No?

Vyn Reese: If they're in…

Jeff Thompson: Mental…dental pressure applied relentlessly.

Vyn Reese: If they're in my practice I'll be happy to call them.

Jeff Thompson: Actually, I have released the list to WIZMA(?) and to the University of Washington. If there's any other clinics that would like a list of their docs, which includes not of the 824, but a full list, just let me know. And this is getting back to the issue about more information is better, so if you would like to represent, you know, your clinic, I can give you these types of things for all your prescribers. I just need a list of names and NPIs and DEA numbers. And we've actually done that for the University of Washington and Harborview.

Patti Varley: Is this…is this on the website? The RX.WA.GOV?

Jeff Thompson: Did we ever post it?

Duane Thurman: Not yet.

Jeff Thompson: Okay.

Siri Childs: But it will be on yours.

Duane Thurman: We'll coordinate.

Jeff Thompson: Yeah.

Vyn Reese: Is that it?

Jeff Thompson: Thank you, Jeff.

Vyn Reese: Thank you very much, Jeff. Don't feel like that we're on you. This is all good work, okay? And it's just we're trying to make it better.

Jeff Thompson: You publish something and have people publically humiliate…

Vyn Reese: I know but don't…no, no. We're agreeing with the message. We're trying to get it to be…

Jeff Thompson: No, these are all really good suggestions.

Vyn Reese: To honed in, to really, you know, busy doctors who don't want to read more than one page, you know.

Siri Childs: I would like…this is Siri again, and I'd like to tell you what we are planning to do for February. If you remember, several of our meetings in the past we've brought to you our plans to look at narcotics more closely. And in February, we would like to bring our two narcotic review nurses to do a presentation to you to let you know what we have discovered, and, you know, the successes that we've had in our narcotic review program. So stayed tuned.

Vyn Reese: We'll look forward to it. So we're now adjourned. Is that right? Thank you. What?

Man: [inaudible]

Carol Cordy: Public comments?

Vyn Reese: Oh, right now?

Vyn Reese: Okay, well, you have one? Sure.

Man: Well, I [inaudible] I just…I understand the question. I…and I wanted to still [inaudible] with Johnson & Johnson. Okay. And I wanted to follow-up on points that [inaudible].

Siri Childs: Can you go to the…

Vyn Reese: Get the mic, yeah.

Male: Excuse me, I'm sorry.

Vyn Reese: Up above you.

Male: Get the one up there.

Barak Gaster: Up the steps.

Male: Up there…there you go. We'll send you in the track.

Bill Strike: This is not easy, but I wanted to follow-up on a point that they made. And for the record, in case it wasn't picked up, my name is Bill Strike and I'm with Johnson & Johnson. On page 4 of the Generic News, on long-acting opioids, I've read the verbiage that occur on…in the left-hand column, and it shows methadone to be the least expensive and methadose, but it doesn't reference the recent CDC MMM report that showed that there was a problem with long-acting opioids in our state which we're all aware of, but it named methadone as being the agent most frequently associated with mortality. And I'm wondering, by having that, you know, Dr. Reese, you said, you would probably go to the least costly. Reasonable assumption. But without disclosure of that fact, are we making informed decisions?

Vyn Reese: This is Dr. Reese. One of the things about methadone was it…it became an increasing problem with overdoses, because it wasn't a preferred drug. Once it began a preferred drug, it was used more, and then it became more common in the community, then there were more overdoses. So there's a lot of…

Bill Strike: Yeah, that's so…

Vyn Reese: It depends on which drug is being used at the time, and so once it was generic and it was pushed as a generic and the State's preferred…on the State's preferred drug list, it was used more commonly, and there were more overdoses from it. It doesn't mean you have to sort of divide that by a denominator. There are more overdoses, yes, that's true.

Jeff Thompson: Well, Bill? Bill? Can I just…I mean, what we don't want to do is…so what I can do is I can put out here; but if you look at the national data on deaths and overdoses, methadone is actually ranked several down from Tylenol with Codeine, Vicodin, and several mental health drugs as being the most likely cause of death from an overdose. So I think what we want to be very careful about, you know, sort of picking on a drug by just

lumping it into a class, so I will be more than happy to actually link the CDC data on, not only what is the most likely cause of prescription overdose, and there is a list from the CDC, but also to continue to point out, you know, where methadone and all the long-acting are so we're not trying to, you know, get a misperception about the dangers, because if you look at the dangers, it's not just methadone. It's some of the other more commonly prescribed, and we already went through the FDA decision to continue to prescribe narcotics with Tylenol which are more likely to produce a death than methadone.

Bill Strike: Yeah. Jeff, that…and I appreciate that. My point was is that when you take a look at the ratio and it shows methadone as being the least expensive and you have a CDC and, I believe, Medicaid HRSA's contributed to the data, I think it's just a note to be cautious and not have an unintended consequence.

Jeff Thompson: Right. And…and that's why I mentioned if you read to the left, I mentioned in here that Washington State has the fifth leading cause of prescription-related narcotic deaths.

Bill Strike: Yeah. But I…I don't see…

Jeff Thompson: And if you look at that it's not only due just to methadone.

Bill Strike: No, but 64% are.

Vyn Reese: But…this is Dr. Reese. If you look at the annual days supplied for methadone compared to the others, there's a lot more methadone out there. That's my point. And if there's a lot more methadone, there's going to be a lot more overdoses. So the more the drug is in the community, the more overdoses they're going to be. So there's been a huge push to increase the amount of methadone that's been prescribed.

Jeff Thompson: But, I agree. We will include the entire data in the next set or not maybe this next one but the other one.

Bill Strike: Okay.

Jeff Thompson: Because it is important.

Bill Strike: Thank you.

Jeff Thompson: Great.

Vyn Reese: Now, we're adjourned. Thank you. Well, one more? Okay.

Nate Miles: Nate Miles with Eli Lilly. Jeff, a couple of quick things I wanted to find out. Number one, is there a patient rep on the DUR?

Jeff Thompson: This is the DUR.

Nate Miles: I mean…yeah, a patient…a consumer? A patient representative?

Siri Childs: No.

Jeff Thompson: I'd have to go look. I don't believe…

Duane Thurman: Nate? Are you talking about the…this DUR committee?

Nate Miles? Uh huh.

Duane Thurman: It's comprised under federal law. It's very specific. I can send you the makeup, but it does not account for a consumer representative, and we've tried to form their P&T Committee at its inception to meet the federal Medicaid requirements, and so that's why we have the composition that we do.

Nate Miles: Okay, because I was going to say, if…if they had a concern about that, but one of the things that we've talked about, the patient care on this, under 5892, Duane and Dr. Thompson, you recalled as we were going through the legislative process, one of the things that the legislature said also, is we want to find out not only ways in which we can reduce costs in the drug category, but we can do it in the safest and most efficacious way. And so think that as you put together the tracking that goes through and get very specific about the numbers of people, the types of over or under prescribing of off preferred drug lists versus DAW and all of that, that tracking so that the legislature and others who are reading this paper and this report can also find out what have been those patient outcomes, because I think the legislature was very interested in finding out those so that this…it was more than an exercise on how do we shift all of the

people to generic drugs. It was as well as how do we make sure that patient safety is not encumbered in some of this, and people are putting…being put at risk also from a legal standpoint, some of the doctors and some of the switching and so forth that is happening at pharmacies when doctor's have their liability on the line because they're the ones who wrote prescriptions if it's getting changed. If you have these negative outcomes who's responsible for that? Those are some of the questions that were left up in the air. And so not being able to monitor any of that, not being able to keep track of, "Did we have any special circumstances?" Senator Prentice(?), Senator Franklin and others raised the issue about as it related to especially minority subpopulations. So as we start doing some of the changes, as we start doing some of the push into that what is being happened over there and I think that this is one of those areas and I had one conversation. I've had no more conversations since we had this conversation about what's happening with the minority populations in this. This would be a very good instrument, this report that you're doing, Jeff, of starting to let those doctors what you're starting to see, if anything, along that line. If there's nothing then that's great. We haven't seen any cultural differences or whatever. But if there are some that have been showing up this would be a good document to let that be known in and so as you look at how do you perfect a document this is not to score you at your writing again, but it's merely just to offer a friendly amendment and some ideas so that you don't get to the end of the period, get to the legislature and not have any of that information there that was also asked for specifically under 5892. Okay?

Jeff Thompson: Sure.

Nate Miles: Okay.

Jeff Thompson: Yes.

Vyn Reese: This is Dr. Reese. Is there anybody else who wishes to speak before we can adjourn?

Duane Thurman: One more. Duane.

Vyn Reese: Okay.

Duane Thurman: I just want to thank you on behalf of the agencies and the governor. We try to keep you out of a lot of the politics but a lot of people are aware of the work that you've done and it's well respected and so I want to thank you for another year of hard work and Janet, I want to thank you for your service over time. Maybe you'll come back in a year.

Janet Kelly: Thank you.

Group: Thanks, Janet.

Vyn Reese: We're adjourned.